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LIFE SCIENCES

BIOMEDICAL AND BEHAVIORAL SCIENCES

No. 20

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APPLICATIONS OF MICROBIOLOGY TO AGRICULTURE

Yerevan KOMMUNIST in Russian 1 Oct 81 p 2

[Article by E. Afrikyan, director of the Institute of Microbiology, Armenian Academy of Sciences, corresponding member of the Academy of Sciences: "Job for Bacteria. Science for Agriculture"]

[Text] There is probably no problem of feed production that is not closely linked to microbiology. At the present time, several important directions have emerged in the area of microbiological work on the feed problem.

As far back as antiquity, man knew the processes to produce grain, fermented milk products and wine, which are actually a form of microbiological processing of products. As a result of vital functions of microorganisms, primarily yeast and lactobacilli, products are digested, enriched with proteins, vitamins and other substances; they become more assimilable and nutritious. Digestion and assimilation of feed and food products by animals and man are largely related to the activity of intestinal microorganisms. Digestive processes would be considerably less intensive in the absence of these microorganisms. Hence a tempting idea was conceived, that of artificial microbiological processing of substrates that are difficult to assimilate. We refer to processes of fermentation of rough fodder, straw, treatment thereof with various microbial enzymes, etc. In our country, the production of such preparations has been set up, and use thereof yields a great economic effect.

One of the important directions of modern microbiology is to develop recovery of feed and food protein on the basis of products that have no feed value, for example, gases (carbon monoxide, carbon dioxide, hydrogen, methane), petroleum products (paraffin) and other mineral compounds.

At the present time, microbiological science is successfully solving the problem of industrial, plant production of feed and food products based on nonagricultural resources. In our country, the world's largest microbiological production of protein-vitamin feed concentrates based on petroleum products has been organized.

In collaboration with genetics, biochemistry and other disciplines, microbiology has solved the problem of recovering the most important protein constituents of feed and food products, i.e., amino acids. The "Lysine" Plant in Charentsavan is the pioneer in this branch of the microbiological industry. Addition of the most important amino acids to feed yields a large economic effect in the livestock industry. Suffice it to mention that addition of lysine to feed yields a feed saving of almost 20% and there is a high weight gain by animals.

The advances made by microbiology are so great that many specialists believe that there is a real prospect of producing feed and food products primarily with the use of nonagricultural means in the near future.

The importance of microbiology is unquestionable with regard to augmenting productivity of plants, particularly leguminous ones, which have 2-3 or more times more protein than grain crops. Leguminous crops play a large part in enriching soil with organic nitrogen. Thanks to symbiosis with so-called rhizobia, they have the capacity to bind atmospheric nitrogen and enrich soil with organic substances. Other microorganisms that come in contact with shrubs and trees also have this property. Thus, the process of soil formation in the exposed land of Lake Sevan occurs chiefly by means of expressly such cultures.

Microbiology has an effective soil-enriching product recovered from rhizobia--nitragin, which is used for presowing treatment of leguminous crop seeds. With such treatment, there is an average of 15-20% increase in productivity of these crops.

The Institute of Microbiology of the Armenian Academy of Sciences has been working for many years on development of new and effective nitragin products. Several valuable cultures of rhizobia have been recommended for growing peas, sainfoin and soybeans. Much attention was devoted to developing an effective nitragin product for sainfoin, which is the main fodder crop raised in this republic. Fields thereof occupy more than 40,000 hectares annually. Peat nitragin, developed at the institute and tested under production conditions in different parts of Armenia turned out to be quite promising: it increased sainfoin yield by 20-30%.

Along with productivity, there is also an increase in protein content of the crops and, accordingly, their feed value. Expansion of leguminous crop planting with mandatory use of nitragin is an important reserve for feed production.

Of exceptional interest among leguminous plants are soybeans, which are richest in protein, vitamins and fat. In our country, major measures are being implemented to increase cultivation of this valuable feed and food crop. For several years, studies have been in progress at our institute of problems of recovery and use of nitragin for soybeans. It was established that it is inadmissible to raise soybeans in Armenia without treating seeds with nitragin, and it should be strictly mandatory to use this product here. At the present time, our institute has some effective rhizobia. Use of some of them in recent years has resulted in the production and successful use of nitragin on soybeans. The soybean yield increased by 30-35%.

Microbiological production of feed products with the use of photosynthesizing microorganisms is quite tempting for such a sunny republic as Armenia. Algae that are rich in protein and vitamins, in particular chlorella, are being used extensively for this purpose in Central Asia and some other regions. Carbon dioxide is essential to grow such organisms, and in a number of instances good results are obtained using units for cultivating chlorella where exhaust gases from boiler rooms are blown through them. At the same time, this procedure improves the environment.

In our republic, the Institute of Hydroponics and Agrochemical Problems and Institute of Microbiology, Armenian Academy of Sciences, are concerned with photosynthesizing bacteria. Units have been developed to raise chlorella for animal

feed, for example, the operating installation at the Nairi Livestock Complex. It is imperative to develop such work, paying special attention to creation of completely automated and more productive units of the closed type.

The advances of microbiology and several other disciplines in the area of producing feed and food products from renewable raw material, primarily cellulose and starch, are extremely promising. This direction of work is particularly important in view of the increased cost of petroleum products and other raw material of feed value. Microbiology can recommend to agriculture some simple and economical methods of processing poorly utilized cellulose waste using it as the basis for protein and vitamin concentrates. Methods of dry fermentation are biotechnologically acceptable; they permit running the microbiological process in ordinary feed shops that also exist in our republic.

Studies pursued under the last five-year plan have yielded encouraging data on the microbiological method of enriching starch-containing raw material with protein. Last year, our institute, in collaboration with the Institute of Physiology of the Academy of Sciences, completed studies of the feed value of biomass of new yeast cultivated on starch without prior treatment thereof. The results of tests on tens of thousands of heads of animals showed the high feed value of this product with regard to augmenting weight gain and productivity of chickens.

There are good prospects in a new direction, which involves growing cells and tissues of plants and animals on artificial nutrient media, with growth intensity that is hundreds and thousands of times greater than in their natural habitat. It is imperative to broaden this research in every way so that it can be introduced into practice.

Valuable knowhow has been gained in our country on the use of microbial fermentation in ensilage practice. The efficacy of such ferments also depends on the distinctions of the bacterial culture. A ferment from pentose-fermenting bacteria, which was recovered by Kazakhstan microbiologists, is quite effective for straw and other raw material that is difficult to ensilage. For the last few years, research has been conducted at our institute, under the guidance of L. Yerzinkyan, to find new active lactobacilli for ensilaging. Several cultures can be recommend d for broad practical use.

It should be noted that the absence of the necessary experimental technological base, without which it is actually impossible to implement in practice the scientific advances, is a hindrance to introduction of the results of many of the studies of the Institute of Microbiology into practice. There is a pressing need for implementation in an orderly fashion of a set of measures, with allocation of funds and resources. For example, a large production complex for maximally effective processing and utilization of plant mass and waste is being organized at the Uzvara kolkhoz in Latvian SSR. Microbiological and biochemical processes are being worked out; technological installations have been produced. This work is headed by the Institute of Microbiology, Latvian SSR. The achievements in feed production are so impressive that their knowhow merits the broadest dissemination. In Estonia, where major measures are being implemented to strengthen the feed base, well-equipped laboratories manned by qualified personnel, which conduct work on a modern level, have been opened at many kolkhozes. These examples illustrate how the party's demands for integration of science and production are being met.

Our republic has a powerful scientific potential in the area of microbiology, which is called upon to make a substantial contribution to strengthening and developing this republic's feed base.

10,657
CSO: 1840/504

UDC: 633.14:631.523

DEFECTIVE CARYOPSIS USED AS SIGN FOR SELECTION OF HIGHLY PRODUCTIVE TETRAPLOID RYE GENOTYPES

Moscow DOKLADY VSESOYUZNOY ORDENA LENINA I ORDENA TRUDOVOGO KRASNOGO ZNAMENI AKADEMII SEL'SKOKHOZYAYSTVENNYKH NAUK IMENI V. I. LENINA in Russian No 12, Dec 81 (manuscript received 19 Mar 81) pp 5-7

KUVARIN, V. V., GLUSHCHENKO, I. Ye., academician of the All-Union Academy of Agricultural Sciences imeni Lenin and CHEBOTAREVA, T. M., All-Union Scientific Research Institute of Applied Molecular Biology and Genetics

[Abstract] Experiments were conducted with 29th-30th generation of Petkusskaya tetraploid rye received from GDR in 1961, which has been used for genetic and breeding work in the USSR since 1963. Seeds were planted and raised in 1978 at the Republic Experimental Hop Growing Station and in 1980 at the experimental base, Gorki Leninskiye, of the All-Union Scientific Research Institute of Applied Molecular Biology and Genetics. Plants were classified according to quantity of defective caryopses and the findings processed on a Mir computer; the effects of defective caryopsis on spike productivity and fullness of seeds, as well as data on spike length, flowers per spikelet, grains per spike (total and defective) are listed in tables. Grain content of the spikes was related to formation of defective grains. There was considerable variation of defective grains. There was considerable variation of defective caryopsis content of different plants, ranging from 0 to 38% per spike. The occurrence of defective caryopsis is a cytogenetic process that causes expression of important features of rye. Highly productive genotypes of tetraploid rye, special attention being given to high grain content, smooth and even grain, absence of defective caryopsis, must be screened, and this is already being done with Petkusskaya tetraploid rye and Tetraploid 1, developed by hybridization of perennial rye and tetraploid forms. References 6: 4 Russian, 2 Western. [503-10,657]

UDC: 633.16:537.531

EFFECTS OF ^{60}Co GAMMA RADIATION ON POLYPHENOL COMPOUNDS IN BARLEY ONTOGENESIS

Moscow DOKLADY VSESOYUZNOY ORDENA LENINA I ORDENA TRUDOVOGO KRASNOGO ZNAMENI AKADEMII SEL'SKOKHOZYAYSTVENNYKH NAUK IMENI V. I. LENINA in Russian No 12, Dec 81 (manuscript received 30 Jul 80) pp 9-11

VILENSKIY, Ye. R. and SHCHERBAKOV, V. K., All-Union "Order of Lenin" and "Order of People's Friendship" Scientific Research Institute of Plant Growing imeni N. I. Vavilov, Moscow Department

[Abstract] Flavones and phenolcarboxylic acids referable to o-diphenols are the main phenol compound groups in barley leaves, with insignificant amount in reproductive organs (spikes). Studies were made of levels of saponarin, flavone glycoside, luteolin glycoside, trihydroxyflavone glucoside and "tritsin" [?] levels before and after exposure to gamma radiation in barley leaves at different stages of organogenesis. Moskovskiy 121 barley was raised in vegetation vessels and exposed to radiation from an experimental "Gamma Field" unit in a dose of 13 Gy at the rate of 0.81 Gy/h. O-diphenol content was assayed without irradiation, 3 and 24 h after irradiation at different stages of organogenesis and its level in leaves at the 4th stage of organogenesis after irradiation. Barley leaves were found to be the most responsive to gamma radiation, with regard to capacity for postradiation production of flavones, at the 4th and 7th stages of organogenesis. There was a 150-200% increase in amounts of the main C-glycosyl flavones, as compared to the control, at these stages. The most drastic increase in leaf o-diphenol content after irradiation was in the 7th phase of organogenesis and in level thereof in generative organs at the 9th phase. Figures 2; references 9: 8 Russian, 1 Western.
[503-10,657]

UDC: 637.086.26

WINTER CATCH CROPS AS GREEN FODDER FOR SPRING

Moscow DOKLADY VSESOYUZNOY ORDENA LENINA I ORDENA TRUDOVOGO KRASNOGO ZNAMENI AKADEMII SEL'SKOKHOZYAYSTVENNYKH NAUK IMENI V. I. LENINA in Russian No 12, Dec 81 (manuscript received 17 Feb 81) pp 12-14

PROSKURA, I. P. and VASYURA, S. A., Ukrainian Scientific Research Institute of Animal Feed

[Abstract] Studies were conducted in 1974-1978 on the experimental plot of the Ukrainian Scientific Research Institute of Animal Feed. Catch crops were

planted after winter grain crops. The following cultivars and varieties were used: Nemerchanskiy 2268 winter rape, Verkhnyacheskaya tetraploid winter rye, Zarechanskaya green hay ["zelenoukosnaya"?], Amphidiploid 1 triticale, Mironovskaya 808 winter wheat and Dneprovskaya 1 winter vetch, using two types of mineral nutrition. Optimum mowing time distribution, height of catch crops at green fodder stage, their productivity, amount of feed recovered from these crops as a function of time at which they are used are tabulated. An increase in mineral fertilizers was found to be one of the means of increasing productivity of green fodder crops for the spring. One can provide for a continuous supply of fodder by planting several crops differing in mowing time, gathering each at its optimum time and obtaining high productivity per hectare.
[503-10,657]

UDC: 631.526(252.6)

HERBICIDAL EFFECT OF PEAT ON FARM CROPS

Moscow DOKLADY VSESOYUZNOY ORDENA LENINA I ORDENA TRUDOVOGO KRASNOGO ZNAMENI AKADEMII SEL'SKOKHOZYAYSTVENNYKH NAUK IMENI V. I. LENINA in Russian No 12, Dec 81 (manuscript received 19 Jun 80) pp 17-18

KASPIROVA, T. A., All-Union Scientific Research Institute of Plant Protection

[Abstract] Studies revealed that diseases occurring in several regions of the northwestern Nonchernozem in tomatoes, cucumbers, cabbage, raspberries, grain crops, pine seedlings and gloxinia were caused by peat used exclusively or as a component of fertilizers or hothouse soil. The damage is similar to that caused by herbicides, but not identical. A comparison is made of the effects of peat, sodium trichloroacetate and dalapon [herbicide] on growth of root systems and stalks of pea, barley and wheat sprouts in laboratory, hothouse and field experiments. Effects of aqueous and alcohol peat extracts were tested, the former having the maximum herbicidal effect. Peat had a stronger effect on stalks of wheat and peas than sodium tricholoracetate, but less marked effect than dalapon on pea stalk length, whereas both herbicides and peat inhibited root growth. Analysis revealed that peat and peat extracts affected plant development showing the same structural changes in tissues as herbicides. It is assumed that biotic and abiotic factors could create favorable conditions for expression of peat's effects on farm crops, and it is difficult to predict them. It is recommended that peat be used in soil mixed with earth, sand and others (manure, shavings, lignin, etc.) to minimize the danger to plants. Figures 2; references 6 Russian.
[503-10,657]

UDC: 636.2:612.822.3

RADIOTELEMETRIC STUDY OF ACTION CURRENTS OF COW'S BRAIN

Moscow DOKLADY VSESOYUZNOY ORDENA LENINA I ORDENA TRUDOVOGO KRASNOGO ZNAMENI AKADEMII SEL'SKOKHOZYAYSTVENNYKH NAUK IMENI V. I. LENINA in Russian No 12, Dec 81 (manuscript received 7 Jan 81) pp 20-22

NAUMOV, A. R., ZUSMANOVSKIY, A. G. and BYKOV, V. P., Ul'yanovskiy Agricultural Institute

[Abstract] The transition to industrial livestock farming technology makes it necessary to have criteria for assessing optimum animal upkeep conditions that would permit optimization of technology, for which purpose physiological parameters have been recorded on livestock, using radiobiotelemetry, which permits picking up, transmitting and recording signals of bioelectrical activity, such as the EKG, EMG and EEG. The hardware of this system is described and samples of the cow's EEG tracings are illustrated. A correlation was found between peaks of EEG activity and milking: one peak corresponds to start of milking and secretion of oxytocin and the second to dissociation between cisternal pressure and milking machine vacuum, which drops toward the end of the milking process and elicits unpleasant, painful sensations that stimulate the animals. The EEG reverts to normal 5-7 min after disconnecting the milking machine. The findings indicate that the EEG of cows reflects different physiological states, changing when they differ from resting activity and reverting to normal when excitatory or inhibitory factors affecting bioelectrical activity of the brain are removed. Figures 3; references: 8 Russian. [503-10,657]

UDC: 636.2:637.512.7

QUALITY OF VEAL FROM INTENSIVELY RAISED CALVES

Moscow DOKLADY VSESOYUZNOY ORDENA LENIMA I ORDENA TRUDOVOGO KRASNOGO ZNAMENI AKADEMII SEL'SKOKHOZYAYSTVENNYKH NAUK IMENI V. I. LENINA in Russian No 12, Dec 81 (manuscript received 1 Oct 81) pp 33-35

AMERKHANOV, Kh. A., All-Union "Order of 'Honor Badge'" Correspondence Agricultural Institute

[Abstract] Comparative studies were made of uncastrated bull calves of the Swiss (1st group, control), Aberdeen Angus (2d group), Kalmytskaya (3d group) and Hereford (4th group) breeds, at the Belorechenskiy Sovkhoz in Kabardino-Balkarskaya ASSR in 1979-1981. There were differences between breeds in feed intake, live weight, relative growth rate, chemistry of meat samples, protein/fat ratio, caloric value per kg veal, relative bone weight. Relative growth

rate at different stages of development from birth to 18 months, morphological composition of carcasses, chemical composition of ground meat samples at 18 months of age are tabulated. The 2d and 3d groups were rated highest for the tenderness criterion, but all groups had a good rating for flavor. Also, all groups reached a large live weight and yielded good quality of meat when raised intensively on tethers. References 11: 8 Russian, 3 Western.
[503-10,657]

UDC: 614.31+614.72:615.918:582.28

NEW DATA ON METABOLISM AND ACTION MECHANISM OF MYCOTOXINS

Moscow VESTNIK AKADEMII MEDITSINSKIKH NAUK SSSR in Russian No 1, Jan 81 pp 88-95

[Article by V. A. Tutel'yan and L. V. Kravchenko, Institute of Nutrition, USSR Academy of Medical Sciences, Moscow]

[Text] The discovery of a large number of mycotoxins, which are secondary metabolites of mold fungi that contaminate foods and feed, evidence of their health hazard to man and animals have led to increasing attention being given to the problem of mycotoxins by specialists in the most varied branches of science. At the present time, more than 240 strains of different species of microscopic fungi have been isolated, which produce about 100 toxic compounds that are the cause of alimentary mycotoxicosis in man and animals (Stoloff, 1976; Gigler, 1978; Weiss, 1978; Wilke, 1979).

Ergotism, toxic alimentary aleukia, cardiac form of beriberi, Reye's syndrome, juvenile cirrhosis of the liver, as well as balkan nephropathy, pellagra and Kashin-Bek disease are among the human diseases whose etiology is related to intake of food contaminated with mycotoxins (Newberne, 1974; Lafont and Lafont, 1978; Ryan et al., 1979; Schoental, 1980).

A number of mycotoxins have marked carcinogenic, teratogenic and mutagenic properties. Aflatoxins, sterigmatocystin, ochratoxins, trichothecenes and zearalenone are notable among the mycotoxins for their toxic effects and wide distribution, although many others are also potentially dangerous to man.

One of the most important medical aspects of the mycotoxin problem is to study processes of biotransformation of mycotoxins in the organism and the mechanism of their effects.

The alimentary route is the principal route of entrance of mycotoxins, with contaminated foods of plant origin or through the system of alimentary chains with milk and tissues of animals which consumed contaminated feed.

What is the subsequent fate of mycotoxins in the body? It has been proven that they can be detoxified by means of biotransformation into inactive compounds, or formation of conjugates with cysteine, glutathione, glucuronic and sulfuric acids; they can accumulate in tissues, remaining unchanged for a long period of time; finally, they can be "activated," i.e., transformed into more active and toxic metabolites (Campbell and Hayes, 1976; Patterson, 1977a, b; Shank, 1977).

First of all, we should discuss aflatoxins that are metabolites of fungi of the genus Aspergillus, whose hepatoxic and hepatocarcinogenic effects have been proven on most animal species (A. A. Pokrovskiy et al., 1977; Lafont and Lafont, 1978). There is also every reason to believe that the high incidence of primary cancer of the liver in some parts of the world is attributable to a high level of contamination of foodstuffs with aflatoxins (Newberne, 1974; Campbell and Stoloff, 1974; P. Lafont and J. Lafont, 1978).

In addition to the four main representatives of the aflatoxin family--aflatoxins B_1, B_2, G_1 and G_2--there are several derivatives--aflatoxins M_1, M_2(isolated from milk), P_1 and Q_1, the most toxic of which is aflatoxin B_1. Studies of the rate of metabolism of aflatoxin B_1 in different animal species revealed that its half-life in the organism constitutes 12-15 h (Mabee and Chipley, 1973). Regardless of route of administration, aflatoxin accumulates rapidly in the liver (Garner and Wright, 1975; Chou and Marth, 1976; Ueno et al., 1980).

Studies conducted in recent years, both in vivo and in vitro, using homogenates and fractions of hepatic microsomes from different species of animals and man revealed that aflatoxins are metabolized by the same enzymatic systems as other xenobiotics (Patterson, 1977a, b; 1979; Shank, 1977). As can be seen in Figure 1, aflatoxin B_1, with the involvement of microsomal oxidases with mixed function, can be subject to hydroxylation with production of less toxic metabolites--aflatoxins M_1, Q_1 and P_1. For many biological species, aflatoxin M_1 is one of the main metabolites demonstrable in milk and urine, although it constitutes no more than 3% of the given amount of aflatoxin B_1 (Shank, 1977; Campbell and Hayes, 1976).

According to the data of Masri et al., aflatoxin Q_1 is the principal product of detoxification of aflatoxin B_1 in the liver of primates and man. Its toxicity is 1/18th that of aflatoxin B_1 (Hsieh et al., 1974; Masri et al., 1979).

Aflatoxin P_1 constitutes about 20% of the given total dose of aflatoxin B_1 and 60% of all of its derivatives demonstrable in simian urine. Of this, 50% is referable to glucuronide and 10% to aflatoxin P_1 sulfate (Dalezios et al., 1971).

The second possible route of detoxification of aflatoxin B_1 in the liver is reduction [recovery] of cyclopentenone with the participation of cytosol dehydrogenases and production of aflatoxicol. This reaction is reversible, for which reason some authors consider aflatoxicol as a "spare" form of aflatoxin B_1 in the cell (Scott and Sinnhuber, 1978; Wong and Hsieh, 1978).

Finally, aflatoxin B_1 can be "activated" with the involvement of the same enzymatic systems of the endoplasmic reticulum. It is believed that one of these "active" forms of aflatoxin B_1 is its hemiacetal--aflatoxin B_{2a}, which readily forms Schiff bases with amino acids, peptides and proteins including, of course, enzymes (Ashoor and Chu, 1975; Patterson, 1979).

It is assumed that 2,3-epoxy aflatoxin B_1 is another "active" form of aflatoxin B_1 (Campbell and Hayes, 1976; Garner, 1975; Swenson et al., 1973, 1975; Patterson, 1979). Although this compound has not been isolated, there

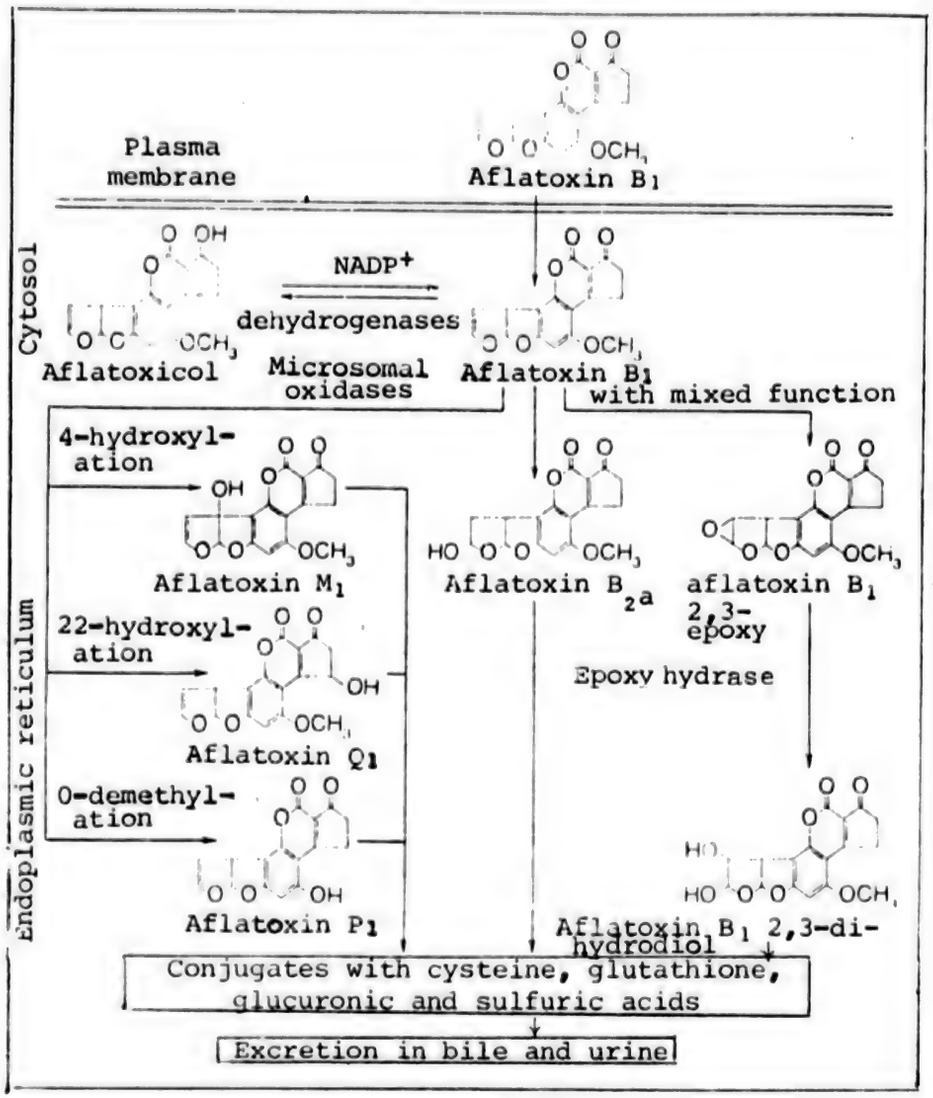


Figure 1. Routes of metabolism of aflatoxin B_1

is considerable convincing indirect evidence of its involvement in the biochemical effects of aflatoxin B_1. The mechanism of metabolic epoxidization has been little-studied, although there is no question that such a reaction does exist in mammalian cells. By analogy with other potent carcinogens (for example, polycyclic aromatic hydrocarbons), it is believed that the dual bond of the terminal furane ring of molecules of the most toxic representatives of the aflatoxin family--aflatoxins B_1, G_1 and M_1--is subject to epoxidization (Schoental, 1970; Campbell and Hayes, 1976). It should be noted that aflatoxins B_2 and G_2, whose molecules do not have these dual bonds, have considerably less biological activity. The 2,3-epoxy of aflatoxin B_1, which is produced under the influence of the enzyme, epoxy hydrase, can change very rapidly into 2,3-dihydrodiol of aflatoxin B_1 (see Figure 1).

This compound, as well as other derivatives of aflatoxin B_1, which are formed in the endoplasmic reticulum, can form conjugates with glutathione, cysteine, glucuronic or sulfuric acids, and then be excreted in this form in bile and urine (Dalezios et al., 1971; Patterson, 1976; Degen and Neuman, 1978).

It is important to note that the direction of aflatoxin metabolism can change significantly, depending on diet. In particular, it was shown that an increase in share of protein in the diet (up to 62%) leads to depression of activity of enzymatic systems responsible for detoxification of aflatoxin B_1, but activation of enzymes that cause its "toxification" (Lee et al., 1978). At the same time, in the case of a protein-deficient (5%) diet, a decrease was demonstrated in activity of epoxy hydrase and amount of cytochrome P-450, with decreased production of aflatoxins Q_1 and M_1 (Adekunle et al., 1978).

Obviously, questions of so-called activation of aflatoxin in the cell are rather important to understanding of the action mechanism of mycotoxins. As we have already mentioned, the deciding factor in the mechanism of action of aflatoxin is interaction, in the first place, of its active form--aflatoxin B_1--with amino acids and proteins, and in the second place of 2,3 epoxy aflatoxin B_1 with nucleic acids.

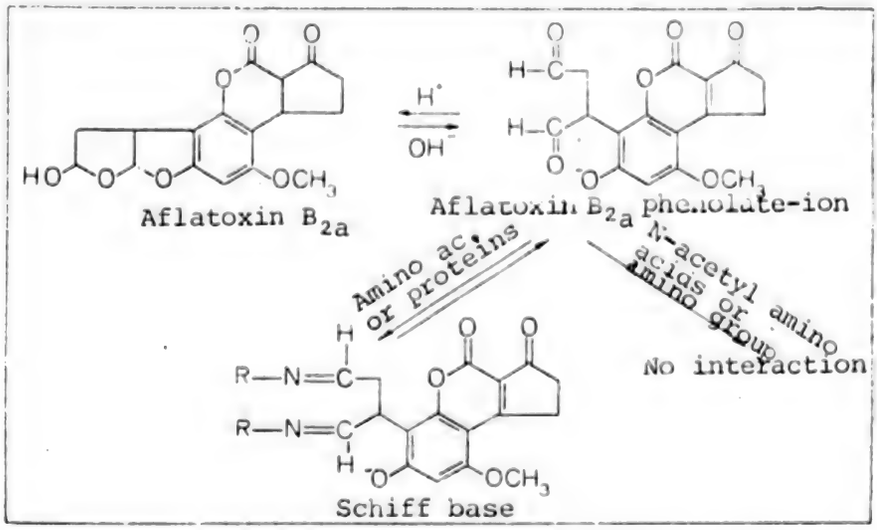


Figure 2. Mechanism of interaction between aflatoxin B_{2a} and amino acids or proteins

The possibility of interaction between aflatoxin B_{2a} and amino acids (Figure 2) implies that phenolate ion thereof is formed in an alkaline medium, and its aldehyde groups interact with amino acid amino groups, forming a Schiff base (Ashoor and Chu, 1975; Patterson, 1976). Evidently, inhibition of many enzymes in the presence of aflatoxin poisoning is based expressly on this mechanism and it is expressly aflatoxin B_{2a} that is the most responsible for the acute toxic effect of aflatoxin B_1.

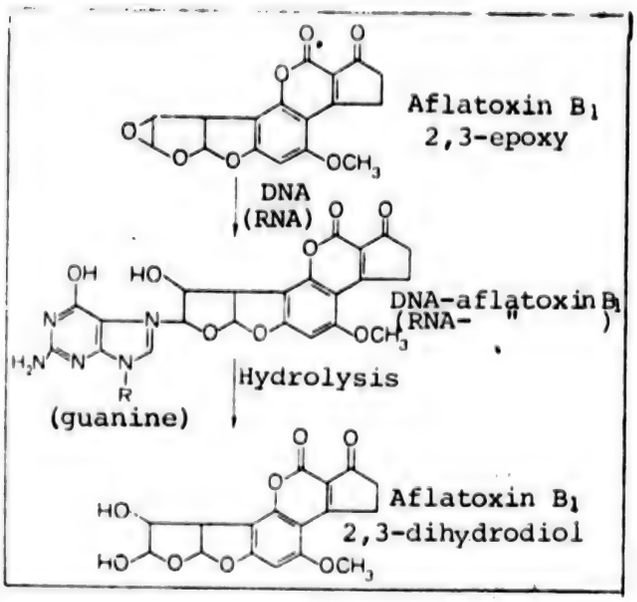


Figure 3.
Mechanism of interaction between aflatoxin B_1 2,3-epoxy and nucleic acids

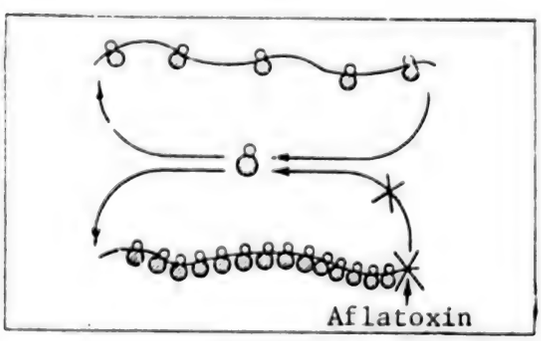


Figure 4.
Aflatoxin-blocked termination of peptide chain synthesis

Aflatoxin B_1 2,3-epoxy, another "active" metabolite, interacts intensively with nucleic acids.

Studies conducted in vivo and experiments in vitro on different models revealed that aflatoxins, like many other hepatotoxins, depress significantly the synthesis of DNA, RNA and protein. It is believed that impaired nucleic acid synthesis is the consequence of interaction between aflatoxin B_1 or its epoxy [epoxide] with the DNA molecule (Figure 3) and impairment of its properties as a template (Wogan, 1974; Swenson et al., 1973, 1975, 1977; Prasanna et al., 1976). Nor can we rule out the possibility of a direct effect of aflatoxins on enzymes of nucleic acid synthesis (Moule, 1974). The studies of Swenson et al. warrant the assumption that a covalent bond is formed between the C-2 terminal furan ring of aflatoxin B_1 (aflatoxin B_1 epoxy) and N-7 guanine (Swenson et al., 1975, 1977).

It is assumed that expressly 2,3-epoxy aflatoxin B_1 is the most responsible for the mutagenic and carcinogenic effects of aflatoxin B_1 (Swenson et al., 1973, 1977; Patterson, 1976; Garner et al., 1979).

The effect of aflatoxin on the process of protein biosynthesis is not limited solely to its interaction with DNA and RNA. It was recently convincingly demonstrated that aflatoxins can block the process of termination of synthesis of the peptide chain (Figure 4). This is associated with impairment of ribosomal movement along mRNA and of the process of their release. So-called spiral polysomes are formed (Sarasin and Moule, 1976).

With reference to the mechanism of action of aflatoxins, we cannot fail to mention their membranotropic effects, particularly the deleterious effect on lysosome membranes. Systematic in vivo studies in experiments on animals and in vitro on isolated organelles of the effects of aflatoxin on lysosomes demonstrated activation of the lysosomal hydrolase complex of target organ (liver) cells and early labilization of hepatic lysosome membranes in aflatoxin-sensitive animal species (A. A. Pokrovskiy et al., 1971; Pokrovsky et al., 1972).

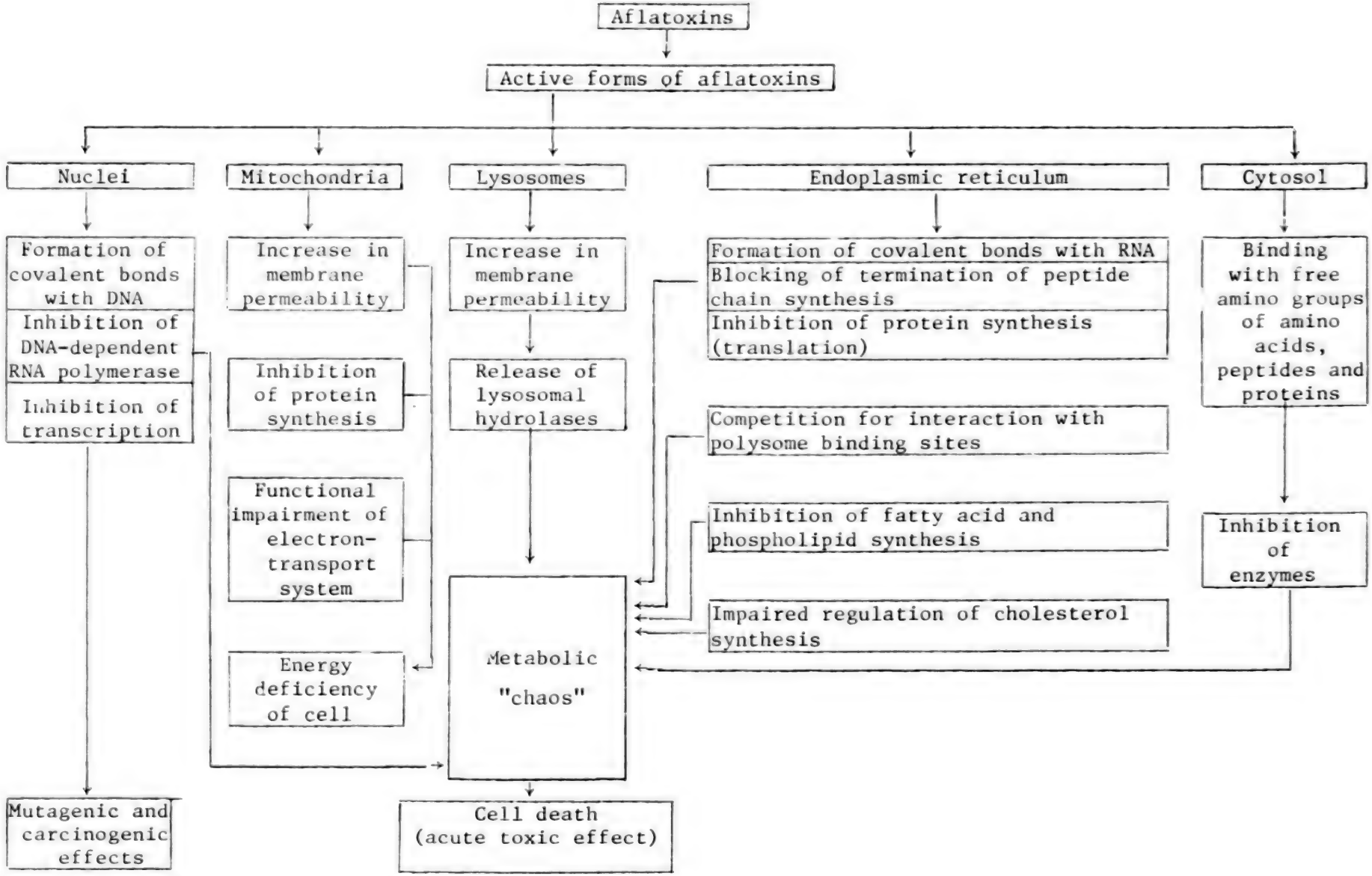


Figure 5. Mechanism of effects of aflatoxins on cell

It can be assumed that membrane structures of the cell, such as lysosomes, may play some part in expression not only of the toxic, but carcinogenic effects of aflatoxins. When released from damaged lysosomes, hydrolases elicit impairment of the structure of other membrane elements of the cell and disorganization of metabolic processes which, perhaps, alleviates to some degree interaction between aflatoxin and the genetic system.

We tried to sum up the current conceptions on the mechanism of aflatoxin action in the form of a chart (Figure 5), which shows that aflatoxins or their active forms affect virtually all cell components.

They bind with DNA in nuclei, inhibit DNA replication, DNA-dependent RNA polymerase and the transcription process proper (Wogan, 1974; Meneghini and Schumacher, 1977; Prasanna et al., 1976); in mitochondria they increase membrane permeability, block syntnesis of mitochondrial DNA and proteins, impair the function of the electron-transport system thus eliciting energy deficiency in the cell (Doherty and Campbell, 1973; Obidoa and Obonna, 1979).

Serious disturbances are observed in the endoplasmic reticulum: in the first place, there is inhibition of protein synthesis due to interaction with RNA and blocking of termination of peptide chain synthesis on polysomes; in the second place, there is successful competition of aflatoxins for interaction with binding sites on polysomes; in the third place, there is inhibition of synthesis and impaired regulation of synthesis of fatty acids, phospholipids and cholesterol (Williams and Rabin 1971; Lo Wan-Bang and Black, 1972; Sarasin and Moule, 1976; Das et al., 1978). As we have already mentioned in cytosol aflatoxin interacts intensively with soluble proteins and inhibits enzymes. Finally, there is the direct effect of aflatoxins on lysosomes, leading to damage to their membranes and release of active hydrolases (A. A. Pokrovskiy et all, 1971, 1972). All of the above factors lead to "metabolic chaos," which precedes cell death.

It could be noted that in discussion of processes of biotransformation of aflatoxins in the body and mechanisms of their interaction, several theses were hypothetical. And this was so, in spite of the profusion of experimental data. As for other mycotoxins, it can be stated with certainty that we are only beginning to solve the problem of identifying the distinctions of their metabolism and action mechanism.

Sterigmatocystin is an intermediate product of biosynthesis of aflatoxin B_1 by cultures of Aspergillus flavus. Like aflatoxins, sterigmatocystin elicits primarily damage to the liver, having a marked mutganeic and carcinogenic effect (Stich and Laishes, 1975; Hamasaki and Hatsuda, 1977). It is believed that in the course of metabolism there is epoxidation of this mycotoxin with production of a highly reactive form, 2,3-epoxy sterigmatocystin (Patterson, 1977b). Expressly this metabolite of sterigmatocystin causes alkylation of nucleic acids, thereby inhibiting protein synthesis (Figure 6). It is remarkable that sterigmatocystin, like aflatoxins, destabilizes lysosomal membranes in the liver. However, it does so to a lesser extent than aflatoxin B_1 (L. V. Kravchenko, 1979). This fact is consistent, to some extent, with the severity of the ultimate

biological effect of sterigmatocystin, the carcinogenic and mutagenic effects of which are less marked than in other representatives of the aflatoxin family.

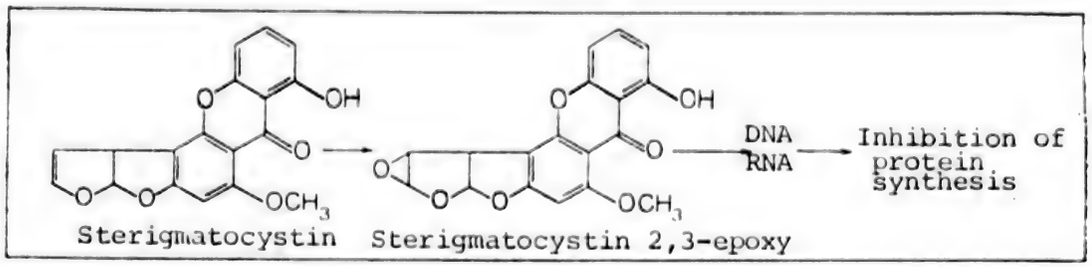


Figure 6. Mechanism of action of sterigmatocystin

The ochratoxin group, which includes toxic metabolites of different species of mold fungi from the genera Penicillium and Aspergillus, merits considerable attention. Structurally, they are isocoumarins bound with L-phenylalanine. Ochratoxins selectively strike the kidneys, mainly the proximal tubules. In addition to the marked nephrotoxic effect, they also have a hepatotoxic effect and teratogenic properties. Some researchers believe that ochratoxins may play some part in the etiology of endemic nephropathy, a serious chronic disease of the kidneys which is widespread in some parts of Bulgaria, Romania and Yugoslavia (Galtier, 1974, 1975; L. V. Kravchenko and V. A. Tutel'yan, 1978; Pavlovic et al., 1979).

Studies of the routes of ochratoxin metabolism revealed that, in rats, 95% of ochratoxin A given per os is bound within 8 h with blood plasma proteins (Galtier, 1974). It is believed that the toxin is accumulated in the liver, kidneys and muscles. However, it is detoxified in the colon, where the intestinal microflora splits phenylalanine from the ochratoxin A molecule through enzymatic hydrolysis (under the effect of carboxypeptidase A) and changes it into a nontoxic product, so-called ochratoxin-α (Galtier, 1975; Chang and Chu, 1977). We cannot rule out the fact that detoxification of ochratoxin A could also occur in various tissues with the involvement of lysosomal enzymes, in particular cathepsin A (Figure 7).

The toxic properties of ochratoxins are attributable primarily to their capacity to bind readily and firmly with proteins (Galtier, 1974; Chang and Chu, 1977; Patterson, 1977). There is information to the effect that they depress synthesis of protein and oxidative phosphorylation (Galtier, 1975; Bunge et al., 1978). It was demonstrated that, in the liver, ochratoxin A depresses phosphorylase b activity and, in the kidneys, leads to depression of gluconeogenesis due to decrease in activity of phosphoenolpyruvate carboxylase (Meisner and Selanik, 1979; Galtier, 1975).

Trichothecene mycotoxins present a significant health hazard to man and animals; they are produced by fungi of the genus Fusarium, as well as some species of Myrothecium, Trichoderma and Cephalosporium. At the present time, there are more than 40 known trichothecenes, producers of which have been isolated from foodstuffs and feed, that were the cause of toxicosis in farm animals and fowl. With regard to chemical structure, trichothecenes are sesquiterpenes (A. N. Kotik et al., 1979; Bamburg, 1976; Schoental, 1980).

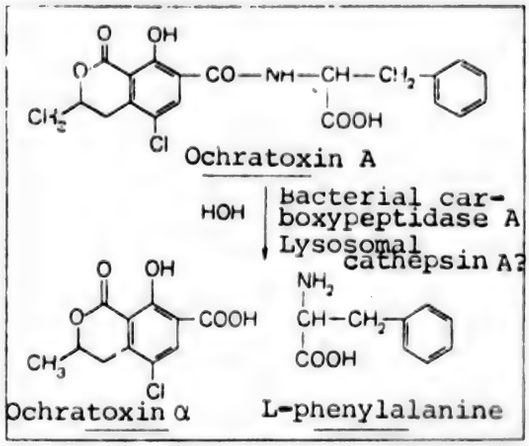
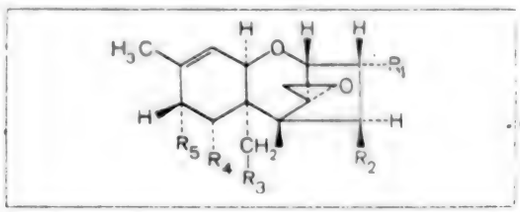


Figure 7.
Biotransformation of ochratoxin A in the organism

Poisoning by mycotoxins of this group is ssociated with involvement of the gastrointestinal tract, cardiovascular and nervous systems, bone marrow and development of the hemorrhagic syndrome (A. N. Kotik et al., 1979; Bamburg, 1976; DeNicola et al., 1978). In other words, trichothecenes have a marked radiomimetic effect. No convincing evidence has yet been obtained of carcinogenic properties in trichothecene mycotoxins (Wehner et al., 1978).

It is believed that the biochemical mechanism of action of trichothecene mycotoxins is based on their inhibitory effect on protein biosynthesis (Bamburg, 1976; Oldham et al., 1980; Agrelo and Schoental, 1980). All of these mycotoxins elicit disaggregation of polysomes and disrupt translation (T-2 toxin, verrucarins, fusarenone X, nivalenol, diacetoxyscirpenol) or the process of elongation and termination of translation (trichothecin, crotocin, trichodermin). It is rather interesting to note that mycotoxins, which depress initiation of translation, have more marked toxic properties than toxins that affect later stages of protein synthesis on ribosomes (see Table). Some trichothecenes are capable of completely depressing the activity of thiol-dependent enzymes (Ueno and Matsumoto, 1975).

Structure of some trichothecenes, toxic properties and effects on protein biosynthesis



Mycotoxin	R_1	R_2	R_3	R_4	R_5	Type of translation inhibition	DL_{50} (for mice, mg/kg)
Verrucarin A, E, F	H	Ether	H	Ether	H	Initiation	0,5—0,75
Fusarenone	OH	OAc	OH	OH	O	Same	3,3
Nivalenol	OH	OH	OH	OH	O	"	4,1
T-2 toxin	OH	OAc	OAc	H	$OOCCH_2CHMe_2$	"	5,2
NT-2 toxin	OH	OH	OAc	H	$OOCCH_2CHMe_2$	"	9,0
Diacetoxy-scirpenol	OH	OAc	OAc	H	OH	"	23,0
Trichothecin	H	OOCCHCHMe	H	H	O	Elongation & termination	250,0
Trichodermol	H	OH	H	H	H	Same	—
Trichodermin	H	OAc	H	H	H	"	500—1000
Crotocin	H	OOCCHCHMe	H		epoxy	"	500,0
Crotocol	H	OH	H		epoxy	"	—

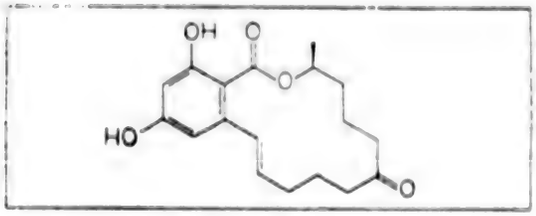


Figure 8.
Structural formula of zeralenone

The few studies that have been made of metabolism of trichothecene mycotoxins are indicative of possible involvement of microsomal enzymatic systems of the liver, in particular, glutathione-S-epoxy transferase (Ohta et al., 1977; Ueno and Ohta, 1977; Patterson, 1977).

Microscopic fungi of the genus Fusarium produce several other mycotoxins, in addition to trichothecens. They include a steroid toxin (produced by F. sporotrichiella) which is the etiological agent of alimentary toxic aleukia (A. A. Pokrovskiy et al., 1976; Pokrovsky et al., 1975). It has been shown that the mechanism of action of this fusariotoxin is based on a membranotropic effect, namely, selective destruction of structure and properties of lysosomal membranes of hemopoietic cells (A. A. Pokrovskiy et al., 1976; Pokrovsky et al., 1975). Some authors believe that, in addition to a steroid fusariotoxin, some part is played by mycotoxins of the trichothecene group in development of alimentary toxic aleukia.

There is one more mycotoxin, zearalenone (Figure 8), a lactone with marked estrogenic properties, which is a metabolite of Fusarium species that are very widespread in nature (Pathre and Mirocha, 1976). When given to rats by mouth, zearalenone is accumulated in maximum quantities in fatty tissue, the myometrium, ovaries and liver (Ueno and Ayki, 1976; Ueno et al., 1977). It stimulates DNA, RNA and protein synthesis in target organs (uterus, mammary glands) (Ueno et al., 1977). It is believed that the biological effects of this mycotoxin are attributable to its capacity to interact with specific estradiol-binding receptors in target cells (Greenman et al., 1977; Boyd and Wittliff, 1978; Mirocha, 1977).

Zearalenone is transformed into α- and β-isomers in the liver, which are more toxic than it is (Mirocha, 1979). It was shown that biotransformation of zearalenone occurs with the involvement of α-hydroxysteroid dehydrogenase, whose activity is demonstrable in both microsomes (NADH-dependent) and cytosol (NADPH-dependent) (Olsen et al., 1979; Tashiro et al., 1979). The formation of conjugates--glucuronides and sulfates--is another route of metabolism of zearalenone and its derivatives, including the more toxic ones (Ueno et al., 1977; Kiessling and Pettersson, 1978; Mirocha, 1979; Olsen et al., 1979).

Thus, we have discussed the routes of metabolism and distinctions of biochemical mechanism of action of several representatives of the rather large mycotoxin group. As could be seen from the submitted data, all of the mycotoxins studied affect to some degree or other the different stages of protein and nucleic acid biosynthesis. But, this is apparently related more to the attention given by researchers to the study of these processes, which are of paramount importance to vital functions of the cell. The demonstrated biochemical changes are not specific to mycotoxins alone, and they do not explain entirely their ultimate biological effects. For this reason, studies of the effects of mycotoxins on other aspects of cell metabolism and, first of all, membranes, which are the structural basis of the enzymatic variegation in the cell and perform an important role in organizing metabolic processes, acquire particular importance.

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EXPERIENCE WITH FRACTION I OF PASTEURELLA PESTIS USED FOR REVACCINATION OF EXPERIMENTAL ANIMALS

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[Article by V. A. Lebedinskiy, Yu. V. Chicherin, V. N. Pautov, V. I. Yevstigneyev, A. A. Byvalov, O. A. Kedrov [deceased] and N. P, Dodonov]

[Text] Refinement of methods and agents for active prevention of plague among residents of endemic regions is still one of the pressing problems of applied immunology. We know from clinical use of the most effective live vaccines that even mass scale administration of such products does not guarantee a radical epidemic-control effect [3, 7]. At the same time, experimental studies have shown that the quality of the vaccine, dosage, route and program of administration are of deciding importance to production of very high immunity to plague. The question of a wise program for vaccination against the plague has been the least studied. In order to work out an effective program for revaccination of the public, it is imperative to expand research on a problem that has not yet been solved. The point is that, on the one hand, with repeated administration of live vaccine, the revaccination phenomenon is possible by virtue of universality--per Zdrodovskiy [2]; but, on the other hand, live plague vaccine may not take in an immune organism and, as a result, there will not be sufficiently strong antigenic stimulation or revaccination effect.

Experimental evidence of both the first and second of these conceptions is offered in the literature. For example, according to the studies of Korobkova [4, 5], there must be 2-fold primary immunization at an interval of 20-25 days, followed by single revaccination every 12 months in order to achieve the required epidemic-control effect, whereas in particularly serious epidemic situations there should be a double inoculation after 6 months. Other authors [8-11, 13] cite experimental data that also confirm that there is a higher level of immunity after two-fold inoculation with live EB plague vaccine and that it is more marked with repeated revaccinations at extended intervals (from 3-4 weeks to 2-3 months), as compared to single immunization.

Conversely, Kotlyarova [6] believes that frequent reimmunization not only enhances resistance to plague, but could drastically lower the immunizing effect. There has been a logical explanation for the decline of immunogenic activity of live vaccine when used for revaccination in the studies of other

authors [12, 14], who demonstrated in experiments on animals that there is "attenuation" of adaptation, as well as rapid elimination, when repeated inoculations are given with immunogenically effective vaccine strain bacteria.

In order to check these theses, as well as find the optimum program for revaccination against plague and choose a vaccine product suitable for this purpose, we conducted experiments on laboratory animals, and the results are submitted here.

Table 1. Protective efficacy of FI and live NIIS vaccine used to reimmunize guinea pigs

Product used for revaccination	Interval between NIIS vaccination and revaccin., days	Number of animals presenting antibodies (numerator) as related to all tested (denominator)	Geometric mean of antibody titer and confidence interval (P = 0.95)	Time between last immuniz. & infection	Effect (of 25,000 LD_{50})		
					Surviving (numerator) animals as related to infected (denom)	I	Time of animal death, days
FI	45	9/9	1:5400×3,7	30	8/9	0,89	14
NIIS vaccine		5/8	1:58×2,1	30	6/8	0,75	14,5
Control 1	—	24/41	1:64×4,2	30	30/41	0,73	7,8
FI	75	9/9	1:10000×3,9	30	8/9	0,89	12
NIIS vaccine		5/7	1:69×1,3	30	5/7	0,71	12
Control 2	—	16/27	1:58×1,9	75	19/27	0,70	10,8
Control 3	—	5/7	1:52×1,9	105	4/7	0,57	10,7
FI	120	10/10	1:41700×4,1	30	10/10	1,00	—
NIIS vaccine		6/8 4/8	1:325×2,7	30	5/8	0,62	10,3
Control 4	—	1:40×2,0	1:40×2,0	150	4/8	0,50	4,8
Control 5	—	0/25	0	—	0/25	0	4,1

Notes: 1. I is ratio of surviving animals to number infected.
2. Vaccination and revaccination was performed by the subcutaneous method, antibody titers were assayed before infection.
3. Controls 1, 2, 3 and 4--animals were not revaccinated; control 5--animals were not vaccinated.

Material and Methods

We used mongrel guinea pigs weighing 280-350 g in our experiments. Primary immunization was administered using NIIS live, dry plague vaccine subcutaneous and by inhalation. The vaccine dosage was 10^5 live microorganisms for subcutaneous vaccination and booster shots and 10^7 live microbes for inhalation. Of the guinea pigs inoculated by inhalation, we selected for the experiment

either specimens with low immunoglobins to fraction 1-FI (1:10 titer) in blood serum, or else none at all, within the range of sensitivity of the reaction of passive hemagglutination (RPHA) of FI antibodies. This was due to the fact that animals with proper serological changes at the early stages (1-3 months) after inhalation inoculation have marked resistance, against the background of which it is difficult to assess the immunogenic activity of vaccines that are intended for revaccination. In this study, we used both live vaccine and a purified preparation (FI) for revaccination. In preliminary experiments, immunogenic activity of FI for white mice, after hypodermic injection together with incomplete Freund adjuvant (IFA), constituted 1.2×2.79 μg (ED_{50} [effective dose]). The booster dosage of such antigen with IFA constituted 100 μg. The intensity of serological alteration in inoculated animals was assessed by the results of the RPHA using FI-sensitized ram erythrocytes. Control infection of animals was performed subcutaneously using 2-day agar culture of P. pestis: dosage of 25,000 LD_{50} to determine the existing number of immune animals [or extent of immunity?] and in the dose range of 10^1-10^7 live bacteria to estimate LD_{50}. We had infected animals under observation for 30 days. Dead animals were submitted to necropsy and bacteriological examination using the conventional techniques for plague infection.

Table 2. Indicators of adaptation ["take"] of live plague vaccine after hypodermic vaccination and revaccination of guinea pigs (M±m)

Vaccination	Number of positive cultures from primary complex on first 3 days after inoculation, %		Concentration of live bacteria/g tissue 3 days after inoculation		Time of last positive culture from first complex, days	Internal organ culture	
	injection site	lymph node	injection site	lymph node		spln	liver
Primary	97±2	86±11	$(113±21)\cdot10^3$	$(26±5)\cdot10^3$	10—15	+	+
Repeated	45±21	23±15	81±40	6±3	1—3	—	—

Notes: 1. Reinoculation was performed 3 months after the primary one.
2. The dosage of vaccine for first time and revaccination was 10^7 live bacteria.

Results and Discussion

Determination of extent of immunity among animals inoculated with vaccine and revaccinated at different intervals with FI and live vaccine by means of hypodermic infection with a massive dose of P. pestis revealed that, in all cases, repeated immunization led to a rise of this indicator (Table 1). Immunogenic activity of FI was higher than the activity of live vaccine, with regard to both protective effect and stimulation of immunoglobulin production. Our findings were also indicative of consistent enhancement of the revaccination phenomenon with increase in interval between inoculations. This pattern was inherent in both live and "chemical" vaccines, but while intensification of the protective effect of the latter was associated with marked serological alterations, when live vaccine was used for reinoculation the increase in

number of resistant animals corresponded to a significaly lower level of antibodies to FI. This can apparently be attributed to the fact that animals, that were inoculated with live vaccine at the long term after vaccination, retained immunity, which prevented adaptation of the vaccine strain of bacteria in a considerable number of animals, but there was not enough vaccine to withstand infection with a virulent culture of P. pestis. In order to verify this hypothesis, we conducted an experiment to study reproduction and dissemination of vaccine strain bacteria in intact and immunized guinea pigs.

Table 3. Intensity of immunity to plague in guinea pigs as related to immunization program

Vaccination program	Animals with antibodies (numer.) of total examined (denomin)	Geometric mean of titer	Infective dose, quantity of live bacteria	Deaths (numer.) out of all infected (denom.)	$LD_{50} \times K$
Inhalation of live vaccine (10^7 live bacteria) and revaccination with FI (100 μg) after 2 months	15/17	$1:470 \times 7{,}3$	10^1 10^3 10^5 10^7	0/4 1/5 1/5 0/3	$>10^7$
Inhalation (10^7 live bacteria)	2/18	1:10	10^1 10^3 10^5 10^7	0/4 2/4 2/5 3/5	$130 \cdot 10^3 \times 128$
Control--animals were not vaccinated	0/15	—	10^1 10^3 10^5	3/5 5/5 5/5	$<10^1$

Note: K--confidence interval of geometric mean with probability of 0.95.

The results of this experiment (Table 2) were indicative of the validity of the above interpretation: vaccine strain bacteria were isolated from the primary complex of revaccinated animals at a lower incidence, in smaller concentration, for a shorter period of time and they were not disseminated in the viscera. Thus, with the second use of live vaccine, apparently the less marked the immunological background due to prior inoculations (longer interval between immunizations), the higher the residual virulence of vaccine bacteria and administered dose of the agent, and the more distinct the manifestation of the revaccination effect. Unlike live vaccine, the "chemical" vaccine elicited a marked revaccination effect in virtually all animals that came out of a refractory state. This effect consisted of intensified immunoglobulin production, larger immune stratum and more intensive immunity. The latter ensues from the following data (Table 3): FI antigen in oily adjuvant used to revaccinate guinea pigs inoculated with live vaccine stimulated production of a significant amount of protective antibodies and increased intensity of immunity by more than a factor of 10^2.

Analysis of the above experimental data leads us to conclude that the task of increasing the intensity of immunity to plague produced by live vaccine and

maintaining it at the proper level for a long period of time cannot be solved by using multiple inoculations of live EB vaccine in the usual doses, because when using live vaccine, due to its poor adaptation in an immune organism, it is difficult to induce manifestation of the revaccination phenomenon--an adequate antigenic stimulation. This problem can be solved by using either "chemical" vaccine for revaccination, which has been confirmed in these studies, or a combination prepared on the basis of live EB vaccine with addition of purified protective antigens, one of which is FI. The efficacy of such a vaccine was demonstrated in the studies of Shmerkevich [15, 16] and Dal'vadyants et al. [1].

Conclusions

1. Inoculation of experimental animals with fraction I of P. pestis with incomplete Freund adjuvant 1.5-4 months after primary immunization with live vaccine causes development of a marked revaccination effect, which is manifested by intensification of immunoglobulin production, increase in the immune stratum [number of immune animals?] and in intensity of immunity.

2. Use of EB live plague vaccine for revaccination provides insignificant stimulation of immunity due to poor adaptation of vaccine strain bacteria in the sensitized organism.

3. The pronounced revaccination properties of fraction I show that it is promising to conduct experimental work to design a "chemical" vaccine against plague, intended for revaccination purposes.

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AFLATOXIN ACCUMULATION IN HIGH-HUMIDITY RICE GRAINS

Moscow PRIKLADNAYA BIOKHIMIYA I MIKROBIOLOGIYA in Russian Vol 28, No 1, Jan-Feb 82 (manuscript received 8 May 81) pp 98-103

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[Abstract] Laboratory investigations were conducted on aflatoxin formation by Aspergillus flavus NRRL 2999 on Krasnodarskiy 424 rice in relation to temperature and humidity of storage. The aflatoxin formation commenced at 15°C, but maximum quantities were formed at 30-35°C and a relative air humidity of 90-95% (18-21% grain humidity). Almost 75% of the aflatoxin was formed on hulled grain: the concentrations of aflatoxin B_1 reached 25300 µg/kg on polished rice, and less than 250 µg/kg on rough rice. In the case of the rice substrate only aflatoxin B_1 was produced. It appears that prevention aflatoxin contamination of rice requires drying the grain in the shortest time possible and maintenance of humidity below the level required for A. flavus growth. Figures 5; references 9: 3 Russian, 6 Western.
[230-12172]

DETERMINATION OF WHEAT RUST RESISTANCE BY DNA/DNA HYBRIDIZATION

Moscow PRIKLADNAYA BIOKHIMIYA I MIKROBIOLOGIYA in Russian Vol 28, No 1, Jan-Feb 82 (manuscript received 10 Jul 81) pp 104-110

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[Abstract] Nitrocellulose membrane filter technique for DNA/DNA hybridization was employed in a search for molecular differences between stem rust-susceptible and resistant varieties of wheat. Studies on 35 varieties of

wheat showed an 86% correlation between the molecular studies and data available from standard field and laboratory observations, indicating the former approach represents a more rapid and convenient method for the evaluation of rust resistance. Differences in the DNA nucleotides sequences between the susceptible and resistant varieties provide a correlation between immunity and genetics at the genome level. Figures 4; references 16: 11 Russian, 5 Western.
[230-12172]

STUDIES OF CHANNEL-FORMATION PROPERTIES IN BLACK WIDOW VENOM

Moscow BIOFIZIKA in Russian Vol 27, No 1, Jan-Feb 82
(manuscript received 10 Feb 81) pp 72-75

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[Abstract] A study was made of the ability of Latrodectus venom to enhance cation permeability, using double-layer phospholipid membranes. It was found that at pH 7.5 the membranes showed high cation selectivity in the presence of the venom. Lowering the pH led to nonmonotonic decline in cation selectivity in channels, finally switching to weak anion selectivity at pH 3.5, suggesting the involvement of carboxyl groups in determination of channel selectivity. Volt-ampere characteristics of the channels were asymmetric and slightly hyperlinear. Channel selectivity differed sharply from channel selectivity formed by alpha-staphylococcus or algal protein; selectivity sequence was $K^+ > Ca^{2+} > Sr^{2+} > Mg^{2+} > Na^+ > Cs^+ \approx Li^+$. It is suggested that the channel selectivity induced by the spider venom may result from the microstructure of the protein component in the channel with a shift in the negatively-charged groups into the "mouth" of the channel under the effect of the field and/or phospholipid changes close to the protein molecule. The possibility that the venom contains certain negatively charged components that block the channels cannot be excluded. Figures 4; references 10: 3 Russian, 7 Western.
[261-9642]

EFFECT OF AEROIONS ON DIRECT AND REVERSE MITOCHONDRIAL ELECTRON TRANSFER IN STRESS

Moscow BIOFIZIKA in Russian Vol 27, No 1, Jan-Feb 82
(manuscript received 11 Feb 81) pp 76-79

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[Abstract] A study was made of the direct and reverse effect of changes in electron transfer in mitochondrial respiration in stressed rats and the effect of aeroions on these indexes. Experimental animals were immobilized for 24 hours and then subjected to the effect of aeroions for 10 minutes; immediately afterward direct electron transfer was studied using the polarographic method and reverse electron transfer using the fluorometric method. In direct electron transfer indexes were determined for added and endogenous succinic acid; in reverse transfer determinations were made of the level of restoration for pyridine nucleotides supported by succinic acid and their lowered levels when substances consuming restored equivalents were administered. It was found that direct transfer was activated and reverse transfer reduced in stress. In oxidation, the acceleration in respiration was even more marked, reaching more than 200 percent of the initial level. Aeroionization of subjects reversed the stress-induced changes. This is the first time that a rapid effect has been seen from moderate therapeutic doses of aeroions, acting to normalize electron transfer in the respiratory chain. Figures 2; references: 6 Russian.
[261-9642]

UDC 681.325.5-181.4:65.011.56:663.18

DESIGN OF AUTOMATED SYSTEMS FOR CONTROL OF TECHNOLOGICAL PROCESSES IN LARGE-SCALE MICROBIOLOGICAL INDUSTRY WITH USE OF MICROPROCESSORS

Kiev UPRAVLYAYUSHCHIYE SISTEMY I MASHINY in Russian No 6, Nov-Dec 81 (manuscript received 9 Sep 80) pp 133-136

[Article by Aleksandr Alekseyevich Oprishko, candidate of engineering sciences, Artem Vartanovich Babayants, candidate of engineering sciences, Valentin Pavlovich Davydov, engineer, Yuriy Grigor'yevich Kolpikov, engineer, and Yakov Asaipovich Khanukayev, candidate of engineering sciences, VNIPI "Promavtomatika" (All-Union Scientific Research and Planning Institute "Industrial Automation"), Groznyy]

[Text] The stable trend toward increase in capacity per unit of technological equipment and intensification of technological processes, which are currently observed [1], are attributable to economic factors of development of the means of production.

The appreciably more complex technology, increased territorial decentralization and correlation between technological units, establishment of more rigid requirements pertaining to protection of the environment from pollution--all this implies that there are rather sophisticated, highly reliable control systems. Unfortunately, the systems that are based on a single central general-purpose computer do not meet the new requirements by virtue of their inherent serious flaws. For this reason, it became necessary to depart from the traditional structure of ASUTP [automated systems for control of technological processes] and change to systems that are partially or entirely decentralized in management structure. This became possible thanks to the advances in semiconductor technology, which enabled ASUTP developers to use new hardware based on microprocessors. The useful qualities of microprocessor equipment best meet the requirements of decentralized control systems.

One of the first hardware complexes (KTS [complexes of technical equipment]), that are functionally complete, compact and productive enough, is the KTS LIUS-2. This is a complex based on microprocessor sets of series K580 and K589, which is directed toward constructing decentralizing control systems with hierarchic architecture in different sectors of industry [2].

The KTS LIUS-2 was used to develop the specifications for an ASUTP for production of protein-vitamin concentrate (PVC) recovered from petroleum n-paraffins.

The technological links between stages were executed with a parallel flowchart.

The equipment for each stage consisted of a group of large similar technological units operating in parallel.

Figure 1 illustrates the structural technological chart for production of PVC from petroleum n-paraffins.

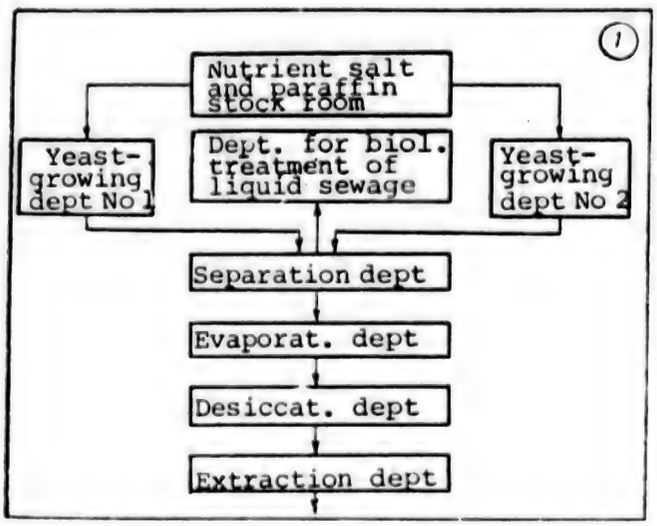

Figure 1. Flowchart for production of feed yeast from petroleum n-paraffins

The raw material (highly purified petroleum n-paraffins, trace elements and salts) are fed into section fermenters 900 m^3 in capacity, where the yeast mass is cultivated. The obtained suspension successively passes through the separation, evaporation, desiccation and extraction departments, in which the end products--feed yeast and biological fat--are isolated. The separated culture fluid is directed for biological purification.

With resepct to software, large-scale production of PVC from petroleum n-paraffins consists of nonuniformly scattered sources and receivers of information over an area of about 3 km^2. In essence, they are concentrated within the production areas according to technological stages. The technological units have 20 to 100 monitoring and control parameters. There is up to 5000 sources and receivers of information in all for the entire plant.

It is convenient to use this industry as an example to discuss the main principles involved in constructing distributed systems for the control of non-continuous biotechnological processes.

Profit is usually taken as the ultimate function of control for this type of industry:

$$D = \sum_{i=1}^{n} (W_i O_i - E_{oi})$$

where W_i is wholesale factory price, O_i is annual output and E_{oi} are operating expenses.

The additivity of the expression for end function enables us to break down the overall criterion into several local criteria according to production stages and different technological units. A correct breakdown guarantees lack of contraction in local and overall control criteria, which makes it possible to operate a decentralized system in parts, thus lowering the initial capital investment. First of all, the parts of the control system can be started up that are instrumental in eliminating the "weak points" of production, yield the maximum economic effect and short pay-off period.

As a result of breaking down the overall criterion, one can single out three groups of control tasks: control of one unit, control of a group of similar units (technological stage) and control of production as a whole.

In accordance with such distribution of tasks, the control system must have three hierarchic levels.

At the next stage of developing the system, it is imperative to solve two main problems first of all: distribution of system functions among control instruments and choice of system architecture.

There may be many solutions to both of these problems for each specific product, and they differ in cost, functional viability, flexibility, speed of operation, etc. Unfortunately, we do not have a formalized method of screening the solution variants at the present time, because there is no generalized criterion for assessing the degree of conformity of an ASUTP to the set goal. For this reason, when screening variants, one uses the heuristic method based on comprehensive evaluation of the features in execution of equipment for the technological process, degree of territorial decentralization of sources and receivers of information, with due consideration of the system's operating characteristics, cost restrictions, etc.

The decentralization principle proposes to make the following separation of functions imposed on the ASUTP [2]: technological channel, i.e., the specific function is referable to a smaller section; according to modes of equipment operation; according to duration of interval for a specific function.

The following general requirements must also be met: required speed of operation and specific time for system reaction to interruptions; physical feasibility.

The typical distinctions of biotechnological processes is the relative independence of operation of technological units within each technological stage. This is the objective basis for distribution of functions on the first control level among control instruments according to technological tag [sign], i.e., monitoring and control functions for each unit should be implemented by a separate microprocessor complex (MPC), containing a microcomputer

and set of peripheral equipment for communication with the controlled process [object] and superior control level.

If there are too many technological units in a group or they are scattered over a large area, it is expedient to break them down into [smaller] groups, and from each to feed information to separate operator consoles. The number of units connected to one console is determined by the permissible sensory load per operator.

Operator consoles are assembled from the KTS LIUS-2 nomenclature, and they consist of the following: microcomputer, multifunction color display, operator's panel and, if necessary, recording device. The microprocessor on the operator's console controls multiplex exchange of information with the MPC of the unit subgroup, and it also effects the communication algorithms with the operator and next higher control level.

The functions of the second control level involve many calculation operations and require high-speed operation and considerable storage in the general-purpose computer. The minicomputers of the future SM EVM series meet these specifications.

Large-scale production in the microbiological industry has a complex structure of information flow. All of the information circulating in the system is divided into production-statistical and operational, and great demands are made of it with regard to delivery time. Accordingly, it is also expedient to separate the hardware on the third control level: one can use the SM EVM to effect gathering, processing and delivery of information to a plant dispatcher and run algorithms of operational-dispatcher control on a real time scale to the greatest effect, but it is convenient to use the YeS EVM for accounting-statistical and economic problems. There should be automatic exchange of information between them via a special communication channel.

In such a structure, the minicomputer processor performs the functions of a communication [linkage] processor, controlling the channels of communication, primary processing and compressing [reducing] information, which makes it possible to relieve substantially the main YeS EVM processor.

After meeting the functional requirements of the system, one must select the optimum architecture based on one of the following schemes: star, circle, trunk line, network, tree.

The parameters of functional viability of the system, as well as expenses for cable production, depend largely on the proper choice of architecture.

In flexible structures, there are features inherent in both centralized and distributed systems. For example, in the separation shop, all of the technological units are concentrated in a small area, and there is an insignificant number of parameters measured and controlled for each of them. Taking this into consideration, it is expedient to increase somewhat the degree of centralization in the system for control of the separation shop, by connecting several separators to each MPC. This provides a gain with regard to expenses for equipment, with negligible loss of system quality.

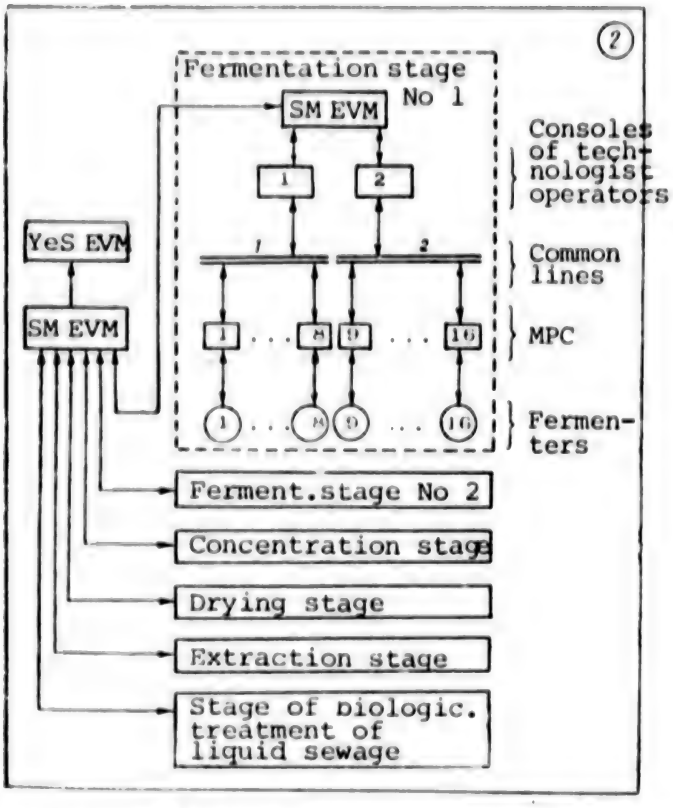

Figure 2. Flowchart of three-level system for control of feed yeast production from petroleum n-paraffins

In order to shorten the needed connecting cables, the control MPC should be located as close as possible to the technological units that they control. There is no need for information links between MPC's, since the units operate independently of one another.

This approach was used to develop the ASUTP for production of feed yeast at the Mozyrskiy Plant. The flowchart is illustrated in Figure 2.

This system has a"tree" and three hierarchic levels of control. The desirability of such a structure in the ASUTP is also confirmed by its analogy to the organizational structures for control of industry, which had been developed for many years.

The first (bottom) level is based on a decentralized circuit with microprocessors for technical units. Each MPC is a microcomputer consisting of a microprocessor, internal storage, PPZU [sequential-access memory unit?] and set of functional elements for communication with controlled process and operator console, combined in an intrablock interface line.

Information about the progress of a technological process is delivered to two operator consoles. Each console is linked with its MPC group by a common OM1 or OM2 line [trunk line?]. The console of the technologist-operator

is equipped with a specialized keyboard,multifunctional color display and recording device.

Upon detection of emergency [accidental] deviations of parameters, at the initiative of the MPC the information is immediately relayed to the operator console, where it is presented on a display and recorded. Upon interrogation by the operator, the information is displayed in an orderly format, in the form of tables, charts and segments of mnemonics.

The second control level has minicomputers with a standard set of peripherals, since the functions on this level involve many calculations and require considerable speed and memory in the general-purpose computer.

The systems for control of stages of separation, evaporation, drying and extraction have an analogous structure--decentralized control for the units, with centralized control for a group of units.

It should be noted that the systems for control of the different technological stages do not execute all of the functions of the first control level to the full extent, but only with regard to the specific problems that are being solved in the systems.

All of the above systems are connected by a system of operational-dispatcher control of feed yeast production; this is the third control level, the functions of which are performed by minicomputers.

This structure has the following features: the element of the top level is a command element in relation to lower level elements, and the decision they make coordinates their action in accordance with the objective of control; the period for decision making is longer for top level elements than lower level ones; the controlling actions originating from a higher element cannot be more frequent than the actions fed to lower elements, whose behavior it coordinates.

A malfunction of some system element does not disrupt the operation of the other elements.

The software becomes simpler and more visible. Since the technological units of one stage are identical, it is sufficient to develop and adjust the software to control one unit, then record it in the permanent memory unit of all MPC of the stage before starting the system. The software can be readily modified throughout the period of operation of the system. Overall productivity of the system can be increased relatively simply by connecting additional MPC's.

This system structure will be introduced in 1982.

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MEANS OF INCREASING PRODUCTIVITY OF COASTAL BIOCENOSES OF SEA AND ADJACENT BASINS

Moscow RYBNOYE KHOZYAYSTVO in Russian No 7, Jul 81 pp 42-44

[Article by A. D. Goncharov, Odessa Union of Fishery Kolkhozes]

[Text] In view of the reduction in natural stock of some commercial maritime species, the question of making wiser use of the biological resources of the coastal region of the Black Sea and limans [shallow estuary regions] is gaining special importance.

One of the means of increasing productivity of coastal biocenoses of the sea and limans is to develop controlled maritime farms for breeding certain species of fish and invertebrates.

In 1974, a team of divers was formed at the Odessa State University to study the structure of biocenoses off the coast of Odessa and in Dzharylgachskiy Bay, as well as distribution of "rapana" [salt-saturated waters?] along the coast of the northwest part of the Black Sea--in Dzharylgachskiy and Tendrovskiy Bays, in the region of Odessa, on the banks of the Dnestr and Shagan. At the same time, observations were pursued of goby behavior in their natural habitat.

The researchers concluded that it is possible to breed some goby species in open type maritime fish farms.

The principle involved in raising gobies is based on their distinctive ecology. Gobies prefer a firm bottom with developed surface, which they use as habitats and spawning substrate. The natural spawning substrate can be well-replaced with an artificial one.

Studies pursued in 1976-1979 revealed that an artificial substrate (motor vehicle tires) is actively populated by fish. By virtue of its large surface area, it provides good living conditions for various hydrobionts, including spawning of gobies and feeding of young fish.

The Odessa Union of Fishery Kolkhozes was concerned with organizing an experimental goby farm to restock this species in the Dnestr liman. The Fishery Kolkhoz imeni P. P. Shmidt, in the southeastern part of the Dnestr liman took on the organization of such a farm.

An artificial reef made up of tires tied together was placed at a depth of 0.9-1.5 m on sandy and mud-sand ground. The reef was 30 m wide and 150 m long. It was perpendicular to the shore. A total of 1000 worn, unusable tires served to construct the reef. As shown by observations, no shifting of the tires was observed due to turbulence of the sea or currents. Nor did they become covered by slime [mud] or sand. The reef is flushed intensively by the current.

Every since the reef was installed, population thereof with fish was monitored. A comparison of the species composition of fish that settled on the reef and inhabit the liman was made on the basis of catches taken near the reef, at a distance of 200 m away. The fish were caught with small trawls, fine-meshed gillnets, stationary trap nets [built on hoops, with net walls] and goby traps.

The species composition of fish in the reef zone did not differ from that of parts of the liman far away from it. There were mainly sand gobies, round gobies [Neogobius melanostomus], whip gobies [Mesogobius batrachocephalus], rufous [brown?] gobies, Neogobius syrman, pike perch, sea perch, roach, white bream, bullheads and pike. However, there was a considerably higher concentration of fish on the reef than in the control section.

The density of gobies on the reef in the spawning period is 160 times greater than in a remote part of the liman. From June to October, there was a 3-5-fold increase in quantity of roach, pike perch of the current year's brood and yearlings, whose stomachs were filled with young gobies; in October to January there was an appreciable increase in quantity of pike who feed on young roach and white bream. There was accumulation of current year's brood of bullheads from the beginning of August to the end of October.

Concurrently, observations of goby spawning were pursued in the region of the reef. Eggs of sand gobies were found on the 80 control tires installed on 20 April. By 8 May, there was an increase in intensity of spawning. Any dense artificial substrate placed on the bottom was covered with egg masses.

The height of sand goby spawning was referable to the period from 8 May to 10 June. It occurred mainly in the daytime, from 1000 to 1700 hours. The roe matured to the "ocellus" [eye] stage within 7-8 days and to the hatching stage within 10-12 days (water temperature 20-22°C). Spawning of round gobies started on 15 June, and it was less intensive than for the sand goby. By 20 August, goby spawning had stopped entirely.

The masses of goby eggs are elliptic in shape. The area thereof ranges from 840 to 2270 cm^2 per tire, constituting a mean of 1200 cm^2. Laying density is 33.2 eggs/cm^2. There was an average of 40,000 eggs per tire. Survival to the hatching stage constituted 97% of the eggs, with at least 90% yield of fry. Loss of eggs from the "clutch" protected by males is attributable to incomplete fertilization and partial consumption by sand hoppers. Unprotected clutches are entirely consumed by other goby males.

The effectiveness of goby spawning on the reef can be calculated by using a formula that we propose:

$$M = \frac{mn\partial 9}{10}$$

where m is mean quantity of eggs per tire, n is number of tires during intensive spawning period and ∂ is the number of periods of complete incubation of roe during intensive spawning.

According to our estimates, M = 27 million goby fry.

After hatching, the fry concentrates in the reef zone, where it finds shelter and feed among the tires overgrown with hydroids and zebra mussels. There are also many small worms, Ostracoda [minute crustaceans], leeches and midges [Chironomidae] inhabiting that area.

At the age of 10-12 days, the goby fry abandons the reef and settles in the adjacent liman waters.

Thus, these studies revealed that a reef made of tires is a highly productive biotope. The profusion of parasites [overgrowth of other material] and necto-benthos provides the necessary feed base for gobies and benthophages that settled on the reef. The large area of the reef surface provides the necessary spawning substrate for gobies, which is many times more effective than the natural one.

The reef zone is a place of intensive feeding [grazing] of pike perch, for which young gobies are a feed component.

Expansion of the reef area (to 10,000-15,000 tires) will make it possible to augment significantly the quantity of gobies in the Dnestr liman, as well as to create an additional feed base for pike perch, make more effective use of liman resources, open up commercial fishing of the sand goby, which is extremely valuable for its gustatory qualities.

10,657
CSO: 1840/267

UDC: 577.391:577.41]46

DISTRIBUTION OF ^{90}Sr and ^{137}Cs AMONG SWAMP-RIVER ECOSYSTEM COMPONENTS

Sverdlovsk EKOLOGIYA in Russian No 2, Mar-Apr 82
(manuscript received 11 Jun 81) pp 45-49

MOLCHANOVA, I. V., KARAVAYEVA, Ye. N., CHEBOTINA, M. Ya. and KULIKOV, N. V., Institute of Plant and Animal Ecology, Urals Scientific Center, USSR Academy of Sciences

[Abstract] This work reports on a radioecological study of one area of a swamp-river ecosystem located 5 km to the southeast of the Beloyarsk Nuclear Powerplant in the Central Urals. It includes a watershed and the flood plain of a small river. Samples of water and bottom deposits of silt, sand and peat were collected in 1978 and studied for content of the radioactive isotopes. It is concluded that the dumping of waste water by the powerplant into the swamp has not resulted in a significant increase in the content of ^{90}Sr. However there is some increase in the content of ^{137}Cs in the swamp, by a factor of 10 to 100, though still two orders of magnitude below the maximum permissible concentration for drinking water. Figure 1; references 9: 8 Russian, 1 Western.
[226-6508]

UDC: 582.271:577.391

INFLUENCE OF THERMAL STATE OF BODY OF WATER ON HYDROPHYTOCENOSES

Sverdlovsk EKOLOGIYA in Russian No 2, Mar-Apr 82
(manuscript received 10 Jun 81) pp 49-55

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[Abstract] A study is presented of the influence of heated water discharge on aquatic vegetation and its predominant formations in a cooling reservoir used

by a Lithuanian regional electric powerplant. Levels of accumulation of ^{90}Sr, ^{137}Cs, ^{144}Ce and ^{10}Pb by plants and soils are determined as a function of temperature, and the effect of elevated temperature on the algae Nitellopsis obtusa is determined. The experiments showed that immediately after cells were placed in heated water their protoplasm mobility increases. However, after longer exposure (about 10 days) the protoplasm mobility decreases sharply in some cells or stops entirely, indicating death of the cells. Model experiments indicated that increasing the water temperature to 25-29°C had little influence on accumulation of ^{90}Sr and ^{137}Cs in algae and macrophytes. Accumulation of ^{144}Ce in aquatic plants was somewhat increased by higher temperatures. The toxic effect of heavy metals on hydrobionts is increased by higher water temperatures. The number of major plant formations in heated water was reduced from 11 (in natural water) to 6. 59 species of macrophytes were reduced to 26. The same plants predominated in both cases. Heated water has a negative influence on most types of aquatic plants, particularly those with floating leaves and Characeae. Myriophylleta spicati and Ceratophylleta demersi as well as Potamogeton perfoliati developed better and formed larger masses in heated areas. References 21: 17 Russian, 4 Western.
[226-6508]

UDC: 599.322.2:591.5(479)

BIOLOGY OF CITELLUS MUSICUS (RODENTIA, SCIURIDAE) IN CENTRAL CAUCASUS

Moscow ZOOLOGICHESKIY ZHURNAL in Russian Vol 61, No 3, Mar 82
(manuscript received 25 Feb 81) pp 419-427

YEMEL'YANOV, P. F., VAGNER, I. K., KARMOV, A. M., TITOV, E. K., IVANOVSKIY, V. V., and VASIL'YEV, N. N., Scientific Research Anti-Plague Institute of the Caucasus and Transcaucasus, Stavropol'; Kabardino-Balkarskaya Anti-Plague Station, Nal'chuk

[Abstract] Observations performed in 1973-1977 and in 1979-1980 in the territory adjacent to the Chegem River Valley have provided additional information on the biology of Citellus musicus, the primary carrier of plague in the Elbrus River area. The age and sex composition of the population is charted for the period of 1974 through 1977, showing an overall decline in the population of mature males and females, with an increase in the number of juveniles observed. The seasonal dynamics of animal activity are studied as well as diurnal patterns and intraspecies relationships. Observations made during 1972-1980 show that the plague epizootic process was continuous with no interruptions except for the winter season when the primary carrier is dormant. Figures 4; references 16(Russian).
[253-6508]

UDC 616.981.51-02

CHARACTERISTICS OF ANTHRAX BACILLI ISOLATED FROM SOIL

Tashkent MEDITSINSKIY ZHURNAL UZBEKISTANA in Russian No 3, Mar 82
(manuscript received 24 Sep 81) pp 46-48

RAKHMANOVA, Kh. U., ZAKHAROV, V. B., SABIROVA, G. Sh., ANTONOVA, L. Ye., ADYLOV, D. A., KADYROV, A. M. and KHAKIMOV, N. A., Republic Sanepid Station, Uzbek SSR Ministry of Health; Uzbek Scientific Research Institute of Epidemiology, Microbiology, and Infectious Diseases

[Abstract] Investigation of 1836 soil samples from grazing lands in areas with known cases of anthrax resulted in the isolation of typical anthrax bacilli from 20 such samples (1:1%): 18 strains were isolated after infection of white mice and 2 by strictly bacteriologic procedures. The isolated strains were susceptible to a number of commonly-employed antibiotics. The study demonstrated that biological testing of soil samples, in combination with immunofluorescent antibody techniques and the pearl necklace test, is the most successful approach to the isolation and identification of anthrax bacilli from suspected soils.
[250-12172]

UDC: 599.4:591.9(581)

REGIONAL SPECIFICS OF AFGHANISTAN BAT FAUNA

Moscow ZOOLOGICHESKIY ZHURNAL in Russian Vol 61, No 4, Apr 82
(manuscript received 26 May 80) pp 585-592

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[Abstract] Afghanistan has a great variety of natural conditions. It includes 11 natural regions of relief, climate and vegetation. In all, 39 species of chiroptera are known in Afghanistan, belonging to 17 genera and 6 families. A table lists the species, which are in the families, Rhinopomatidae, Emballonuridae, Rhinolophidae, Megadermatidae, Mollosidae and Vespertilionidae. Studies of the chiroptera of Afghanistan have emphasized the transitional nature of ecologic conditions and the specifics of formation of the animal population of a given natural region. Additional materials must be collected to determine the positions of the biogeographic boundaries of the species. Since all of the rodents and chiroptera provinces of Afghanistan extend into the territory of neighboring states, cooperative analysis of the various groups of animals and improvement of biogeographic regionalization of the entire area on a multinational basis is required. Figures 2; references 26: 4 Russian, 22 Western.
[258-6508]

UDC 616.5-006.04(47+57)

CUTANEOUS MALIGNANCIES IN THE USSR

Leningrad VOPROSY ONKOLOGII in Russian Vol 28, No 3, Mar 82 pp 9-13

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[Abstract] The statistics of cutaneous neoplasia in the USSR were reviewed, which showed that such cancers are third in the incidence of all the malignancies in the USSR (after gastric (1st), and pulmonary (2nd)). The highest incidence of skin cancer is enountered in Estonia (30.6%), Ukraine (28.5%), Latvia (25.3%) and the RSFSR (24.0%), while the lowest figures apply to the Transcaucasian and Central Asian republics. The overall morbidity for this form of cancer for the USSR increased from 20.1% in 1970 to 22.2% in 1977, while the mortality for the corresponding period of time doubled. Figures 2; references 10: 2 Western, 8 Russian.
[228-12172]

UDC 616.988.21-084.47(571.56)

MANAGEMENT OF RABIES CONTROL PROGRAM IN YAKUT ASSR DURING ERADICATION OF ECDEMIC RABIES

Moscow ZDRAVOOKHRANENIYE ROSSIYSKOY FEDERATSII in Russian No 8, Aug 81 (manuscript received 25 Dec 80) pp 23-25

PETROV, P. A., VEGOROV, B. A. and CHERNYAVSKIY, V. F., Yakut ASSR Ministry of Health

[Abstract] A brief survey is presented of the measures employed in Yakutia to control and prevent outbreaks of rabies. The steps taken include a careful epidemiologic work-up and mapping of cases, public education, strict enforcement of laws pertaining to veterinary survey of domestic animals and monitoring of wild animals, and prophylactic treatment of the at-risk individuals, with vaccines and immune gamma globulin.
[252-12172]

IMMUNOLOGIC SURVEY FOR BRUCELLOSIS IN ANGREN

Tashkent MEDITSINSKIY ZHURNAL UZBEKISTANA in Russian No 3, Mar 82
(manuscript received 18 Feb 81) pp 62-63

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[Abstract] Epidemiologic studies were conducted on the urban population of Angren (Uzbekistan) to determine prevalence and immunity against brucellosis. Passive hemagglutination tests revealed that the 6160 individuals examined 36.7% of those employed in meat processing were positive, 27.1% of those residing in areas with cattle brucellosis, 20.2% of the individuals who owned cattle, 9.4% of the dairy workers, and 2.1% of residents not engaged in any manner with the cattle industry. Of the meat workers and residents in areas with cattle brucellosis 9.2% and 6.5% presented with chronic brucellosis, respectively; the corresponding figures for individuals in these categories presenting with clinical complaints characteristics of brucellosis were 15.3% and 14.3%.
[250-12172]

UDC: 612.017.11+616-002.3+547.458.1:616-033.725

ENHANCEMENT OF NONSPECIFIC ANIMAL RESISTANCE TO INFECTION BY POLYSACCHARIDE COMPLEX OF PLANT ORIGIN

Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 5, May 82 (manuscript received 2 Nov 81) pp 89-94

[Article by A. I. Goncharov, Khar'kov Medical Institute]

[Text] Researchers are devoting increasing attention to the problem of effective treatment of diseases caused by pyogenic staphylococci and Gram-negative bacteria (Bacillus pyocyaneus, E. coli, Klebsiella and others), because of their increasing role in human pathology. These microorganisms are widespread at this time, they are notable for great adaptability to environmental factors, natural or acquired resistance to antibiotics. The diseases that they cause are called "opportunistic infections" by some authors, which "flourish under conditions of civilization" [15]. They owe their appearance to attenuation of immunological reactivity of the body under the influence of burns, surgical interventions and various medical procedures, wide and unwise use of antibiotics and hormones that have immunosuppressant effects. It is known that even highly effective agents against infection do not reach their end goal without the direct involvement of protective mechanisms of the body [1, 3, 9, 11].

Agents capable of stimulating nonspecific resistance reactions acquire much importance when there is low systemic resistance. Such agents include liposaccharide and polysaccharide complexes recovered from Gram-negative bacteria [4, 6], yeast [7], Actinomycetes [5], as well as ribonucleic acid preparations.

Polysaccharide complexes of plant origin have a broad spectrum of biological activity, like the agents listed above [10, 12-14]; however, they have still not found application in clinical practice, due to the difficulties referable to technology of producing them, studies of spectrum of biological activity and standardization.

Our objective here was to test the effect of a complex polysaccharide of plant origin on development of nonspecific animal resistance to staphylococcal and B. pyocyaneus infection.

Material and Methods

We made an experimental study of the biological activity of a stimulator of plant origin, which consisted of a complex of polysaccharides and trace

elements. The product contained no protein. This agent is superior to bacterial polysaccharides in that it has low toxicity. Acute toxicity was determined according to Kerber on mongrel white mice weighing 16-18 g, albino rats weighing 100-110 g and 11-day chick embryos. For mice, LD_{50} constituted 647 mg/kg and LD_{100} 1180 mg/kg; for rats the figures were 750 and 1500 mg/kg, respectively. Doses of 5 to 30 mg were found to be nontoxic to embryos. To determine the biological activity of this complex, we tested its effect on development of nonspecific resistance to infection on the model of staphylococcal and pyocyanic infection. The product was given via different routes to mice weighing 16-18 g in doses of 2-10 mg and 1-10 days later they were infected with a lethal dose of 24-h culture of pathogenic staphylococcus (strain 456) or B. pyocyaneus (strain 11). One MLD of Staphylococcus culture consisted of 500 million bacterial cells in 0.4% thin agar, and for B. pyocyaneous it constituted 50 million bacterial cells in saline, which were injected intraperitoneally in a volume of 0.5 mℓ. Under these experimental conditions, the mice developed a severe, generalized septic process, as a result of which 60 to 100% of them expired within 1-10 days.

We assessed efficacy of the complex according to survival and, in the case of staphylococcal infection, also by intensity of contamination of viscera and blood of experimental and control animals. Reliability of differences between experimental and control groups of animals was determined by means of the χ^2 criterion [2]. The differences were considered reliable with $\chi^2 = 3.74$ ($P<0.05$).

Results and Discussion

In preliminary experiments, we tested different doses of the complex when given intraperitoneally and animals were infected 48 h later. The results revealed (Table 1) that parenteral injection of the complex, already in a dosage of 500 μg/mouse, was associated with development of nonspecific resistance to staphylococcal infection, and with increase in dosage to 2, 5 and 10 mg/mouse the survival rate constituted 73.3, 80 and 88%, respectively.

Table 1.
Effects of different doses of complex on mouse survival after septic staphylococcal infection

Dosage	Survival			P
	abs	%	χ^2	
100 μg	4/15	26,6	0,83	>0,1
500 μg	8/15	53,3	5,4	<0,05
1000 μg	10/15	66,6	8,9	<0,01
2 mg	11/15	73,3	11	<0,00
5 mg	12/15	80	13,3	<0,001
10 mg	22/25	88	21,7	<0,001
Control	2/15	13,3		

Note: Numerator--number of surviving mice; denominator--number of mice in test

In the next experiments, different doses of the complex were given intraperitoneally, intramuscularly and subcutaneously, once or three times. Stimulated animals were infected 1, 2, 3 and 5 days later.

The results of these experiments (Table 2) revealed that survival of experimental animals constituted 80-93.3% after single intraperitoneal injection of the complex in a dosage of 2 mg, 1, 2, 3 and 5 days before infection, whereas 70-90% of the control animals died. Single injection of the agent in doses of 5 and

10 mg was also associated with development of high resistance to staphylococcal sepsis, protecting 80-95% of the experimental animals, against the background of 80-100% death among the controls. High resistance developed in mice under the influence of the complex polysaccharide as early as 24 h after administration, and it persisted for at least 5 days.

Table 2. Effect of polysaccharides on survival of mice after staphylococcal infection

Dosage, mode and frequency of administering agent	Survival at different times after giving complex											
	24 h			48 h			72 h			5 days		
	abs	%	χ^2	abs	%	χ^2	abs	%	χ^2	abs	%	χ^2
2 mg IP (intraperitoneally) once	14/15	93.3	14	12/15	80	11.7	14/15	93.3	11	12/15	80	6.25
Control	2/10	20		1/10	10		3/10	30		3/10	30	
P		<0.001			<0.001			<0.001			<0.01	
5 mg IP once				12/15	80	13	14/20	70	20.6			
Control				2/15	13.3		0/10	0				
P					<0.001			<0.001				
10 mg IP once	9/10	90	7.7	19/20	95	21	9/10	90	16.9	9/10	90	7.7
Control	1/5	20		1/10	10		0/5	0		1/5	20	
P		<0.01			<0.001			<0.001			<0.01	
5 mg subcutaneously, once				4/10	40	0.95				8/10	80	7.2
Control				2/10	20					2/10	20	
P						0,1					0.01	
10 mg IP 3 times	17/20	85	22	17/20	85	11				19/20	95	23
Control	2/20	10		3/15	20					2/20	10	
P		<0.001			0.001						<0.001	
10 mg intramusc. 3 times	15/20	75	17	16/20	80	12				15/20	75	17
Control	2/20	10		3/15	20					2/20	10	
P		<0.001			<0.001						<0.001	

Note: Numerator--number of surviving animals; denominator--number of infected animals.

Three intraperitoneal injections or intramuscular injection of the agent 1-5 days before infection were also associated with development of high resistance, protecting 75-95% of the experimental animals from death, versus 80-90% death in the control groups.

Subcutaneous injection of the agent was found to be less effective.

When staphylococcal infection was produced in mice by means of intraperitoneal infection, we usually observed generalization of the process with formation of pyemic sites in the kidneys, liver and mesentery. Special in vitro experiments with staphylococcus cultures demonstrated that the preparation had no antibacterial activity. Consequently, the agent exerted its influence on development of resistance via the protective and adaptive reactions of the organism.

Considering the above-mentioned distinctions of effects of the complex on animals, we conducted macroscopic and bacteriological studies of blood and viscera of experimental and control animals that survived for 10-12 days after infection.

Table 3.
Macroscopic and bacteriological studies of viscera and blood of experimental and control animals

Animals	Number of foci in organs			Results of cardiac blood cultures
	liv.	spleen	mesentery	
Experimental	8/27	8/27	6/27	3/26
Control	7/8	8/8	8/8	4/8
P	<0,01	<0,001	<0,001	<0,02

Note: Numerator--number of mice with pyogenic sites in organs and positive blood culture tests. Denominator--number of animals submitted to necropsy

These studies revealed (Table 3) that many pyemic sites were consistently demonstrable in the liver and particularly the kidneys and spleen of surviving control animals. Not infrequently, the spleen and kidneys were fused by the same pyemic focus. Control animals lost weight and were listless. In cultures and impression smears of organs from control animals, we consistently found overall growth of staphylococci. These studies were indicative of intensive development of a septicopyemic process. Unlike control animals, in most experimental ones we failed to demonstrate formed suppurative sites, and in a few cases (less than one-third), they were demonstrable in the form of isolated fine foci. Cultures of organ material (impression smears) revealed growth of staphylococci in the form of isolated colonies. Blood cultures were positive in 50% of control animals and only 11.5% of experimental ones.

Table 4. Effect of single injection of different doses of the agent on mouse survival after pyocyanic infection as related to route of administration (5 and 10 mg/mouse with parenteral injection and 20 mg/mouse when given by mouth)

Dose	Route	Mouse survival at different times after complex														
		24 h			48 h			72 h			5 days			10 days		
		abs	%	χ'	abs	%	χ'	abs	%	χ'	abs	%	χ'	abs	%	χ'
5 mg	IP	11/20	55	8	18/20	90	22	16/20	80	10	16/20	80	12	9/10	90	16
	C	1/15	6.6		3/20	15		2/10	20		4/20	20		0/90	0	
	IM	8/10	80	7.2	6/10	60	3.3	4/10	40	2.4	7/10	70	10.7	7/10	70	7.5
	C	2/10	20		2/10	20		1/10	10		0/10	0		1/10	10	
	HD	0/10	0		7/10	70	10.7	9/10	90	12.8	9/10	90	12.8	2/10	20	0.3
	C	0/10	0		0/10	0		1/10	10		1/10	10		1/10	10	
10 mg	IP	13/28	46.4	8.8	22/28	78.5	14	26/28	92.8	14	19/20	95	25	9/10	90	11
	C	0/13	0		2/13	15.3		6/15	40		0/10	40		0/5	0	
	IM	8/10	80	13	8/10	80	13	9/10	90	12.8	7/10	70	7.5	4/10	40	2.4
	C	0/10	0		0/10	0		1/10	10		1/10	10		1/10	10	
20 mg	HD	6/20	30	0.3	15/20	75	27	16/20	80	10	16/20	80	10	17/20	85	12
	C	2/10	20		0/10	0		2/10	20		2/10	20		2/10	20	
	PO	5/20	25	3.0	4/20	20	2.3	10/20	50	4.5	6/20	30	3.75			
	C	0/10	0		0/10	0		1/10	10		0/10	0				

Note: Numerator--number of surviving animals; denominator--number of infected animals.

Key: IP) intraperitoneal injection
C) control
IM) intramuscular injection
HD) hypodermic injection
PO) per os

Table 5.
Effect of 3 injections of agent in a dosage of 10 mg/mouse on survival after pyocyanic infection

Time after injection, days	Animals	Survival after giving the complex					
		intraperiton.			intramuscularly		
		abs	%	χ^2	abs	%	χ^2
1	Experimental	18/20	90	31	19/20	95	32
	Control	1/20	5	--	1/20	5	—
2	Experim.	18/20	90	32	13/20	65	19
	Control	0/20	0	—	0/20	—	—
5	Experim.	13/20	65	12	11/20	55	9
	Control	2/20	10	—	2/20	10	—

Note: Numerator--number of deaths; denominator--number of infected animals

Study of the effect of the agent in a dosage of 5 mg/mouse on survival after pyocyanic infection as related to route of administration revealed (Table 4) that resistance developed in the animals as early as 24 h after intraperitoneal and intramuscular injection of the complex, and there was appreciable increase in survival rate of experimental animals as the interval between administration of the agent and infection increased. Resistance persisted 10 days after administration of the product, and at this time it protected 90% of the experimental animals from death when injected intraperitoneally and 70% when given intramuscularly, versus 90-100% death of control animals.

When the agent was given subcutaneously, mouse resistance to pyocyanic infection developed after 48 h and persisted at a high level for 5 days, protecting 90% of the animals from death, versus 90% death of control animals.

Intake of the complex by mouth was less effective than parenteral administration, in spite of the fact that the dosage was increased to 20 mg/mouse.

In the next series of experiments, we tested the effect of different routes of administration of the complex in a dosage of 10 mg/mouse on development of resistance to pyocyanic infection. The results of these experiments (see Table 5) revealed that single intraperitoneal injection of the agent in a dosage of 10 mg/mouse was associated with resistance to infection as early as 24 h after injection, protecting 46.4% of the experimental animals from death. Resistance was significantly increased thereafter, so that 78.5, 92.8, 95 and 90% of the experimental animals survived after 2, 3, 5 and 10 days, respectively, versus 60-100% death of control animals.

After intramuscular injection of the complex, resistance to infection developed in the animals within 24 h and persisted at a high level for 5 days, protecting 70-90% of the experimental animals, versus 90% death of control animals.

Hypodermic injection of the complex in a dosage of 10 mg/mouse, as well as a dosage of 5 mg, was associated with development of high resistance only 2 days later; however, resistance of these animals remained on a high level for 10 days, which was not observed with a dosage of 5 mg/mouse. It can be assumed that the agent is resorbed more slowly when injected subcutaneously, and that it has an effect on cellular and humoral factors of nonspecific protection.

From the practical point of view, it was interesting to test the effects of multiple injections of the complex on development of immunity to infection. For this purpose, one group of mice was given the agent in a dosage of 10 mg injected intramuscular and another, the same amount given intramuscularly for 3 successive days. The animals were infected 1, 2 and 5 days later. The results (Table 5) revealed that three intramuscular or intraperitoneal injections resulted in development of high resistance to subsequent infection of the animals with a culture of B. pyocyaneus in a lethal dose, protecting 55 to 95% of the experimental animals from death, versus 90-100% death in control mice.

A comparative analysis of administration of the complex once and three times revealed that there were no appreciable differences with regard to animal survival.

Conclusions

1. Experimental studies of a complex polysaccharide of plant origin showed it to have low toxicity and high biological activity.

2. Single or 3-fold intramuscular or intraperitoneal injection of the complex in doses of 5-10 mg/mouse before infection was associated with development of high resistance to staphylococcal and pyocyanic septic infection (55-90% of stimulated animals were protected, versus 90-100% death of control animals).

3. Resistance to septic infection developed 2 days after subcutaneous injection of the complex. Intake by mouth was ineffective.

4. Administration of the complex 1-10 days before infection prevented to a significant degree the formation of suppurative sites in internal organs of experimental animals.

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CSO: 1840/232

UDC: 616.9-036.2+579.8]:061.62"1891-1981"

ACHIEVEMENTS AND FUTURE OF SCIENTIFIC RESEARCH INSTITUTE OF EPIDEMIOLOGY AND MICROBIOLOGY IMENI N. F. GAMALEYA, USSR ACADEMY OF MEDICAL SCIENCES (COMMEMORATING 90TH ANNIVERSARY OF ITS FOUNDATION)

Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 5, May 82 pp 116-120

[Article by D. R. Kaulen]

[Excerpt] This rather incomplete list of directions and their originators is indicative, nevertheless, that the problem of finding the means of controlling infectious pathology has been the principal one over the entire long road of formation and development of the IEM [Scientific Research Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, USSR Academy of Medical Sciences]. The many years of development of the above-mentioned directions of research, headed by outstanding scientists and their disciples, resulted in having these directions become traditional for this institute, enabling it to take a leading place among institutes in this field. Expressly this circumstance determined the function of the institute as the chief institution for the following problems of national importance: "Medical Microbiology," "Genetics and Molecular Biology of Bacteria," "Theoretical and Applied Infectious Immunology" and "Endemic Infections." In addition, it is the chief institute for directions such as "Structure, Function and Molecular Mechanisms of Changes in Genetic System of Microorganisms," "Molecular and Biological Bases of Immunogenesis and Biosynthesis of Antibodies," which are under the jurisdiction of the interagency council for molecular biology.

The institute participates in implementation of several interagency, coordinated and combined programs: "The Plasmid," "Cell Cultures," "Scientific and Technological Bases for Territorial Diversion of Water Resources," "Radiation Sterilization," "Diagnosis, Therapy and Prevention of Diseases Common to Man and Animals," "Brucellosis," "Tularemia," "Leptospirosis," "Rickettsiosis," "Interferon," "Tactics of Preventive Vaccination," "Biomedical Research in the BAM [Baykal-Amur Mainline Railroad] Zone," "Rheumatism," "Viral Hepatitis," "The Gene,," "Gene of Interferon" "Immunity and Medical Genetics."

The institute is involved in extensive international collaboration with the People's Republic of Bulgaria, GDR, Hungarian People's Republic, CSSR, as well as France and the United States. It is the coordinator of Soviet-French collaboration in the area of applications of electron microscopy in medicine and biology, as well as collaboration between the USSR and GDR on the problem of "Infectious and Viral Diseases." There are 11 WHO centers and scientific projects based at the institute.

At the present time, the institute has nine departments: epidemiology, endemic infections, general medical microbiology, bacterial infections, bacterial toxins, microbiology of latent infections, structure and function of microorganisms, immunity to viruses and immunology. These departments are comprised of 49 laboratories, in addition to which there are 2 independent laboratories, a scientific management department, department of scientific medical information with scientific library and ancillary scientific sections.

The institute employs about 1000 people, including 311 scientists, among whom there are 81 doctors of sciences and 212 candidates of sciences. There are 6 people with the title of academician and corresponding member of the USSR Academy of Medical Sciences, 38 professors, 2 Lenin Prize laureates, 2 State Prize laureates and 2 with the title of Honored Scientist of the RSFSR.

The IEM is not only the founder of scientific schools and new directions of research. It is a training center for the USSR and foreign countries. Each year, 30 to 50 graduate students undergo training there, 5 to 10 doctoral and 20 to 25 candidatorial dissertations are defended, up to 300 work places are provided for different periods of time to learn new methods of research and conduct joint studies.

A council of young scientists and specialists, consisting of 160 young scientists (33 scientific workers, 81 senior laboratory technicians and 46 graduate students) works actively at the institute.

In 1976-1980, the institute staff published 32 monographs, 15 collections of scientific papers and 2034 scientific articles in the Soviet and foreign press; 10 doctoral and 59 candidatorial dissertations were defended; 23 author certificates for inventions were granted.

The IEM is a consistent participant of the USSR VDNKh [Exhibition of Achievements of the National Economy]. Under the 10th Five-Year Plan, 10 exhibits were submitted to the USSR VDNKh; 3 silver, 13 bronze medals and 27 certificates of VDNKh participants were awarded. An injectable interferon product was awarded a certificate at the international "Public Health 80" exhibition.

Work on 28 scientific projects resulted in introduction of scientific achievements to public health practice under the 10th Five-Year Plan. A total of 89 instructive and methodological materials, 9 instructions and methodological guides were approved by the USSR Ministry of Health and distributed among concerned institutions.

The institute devotes much attention to rendering scientific and practical assistance to public health agencies. Under the 10th Five-Year Plan, a combined plan of measures was developed and implemented, which included the creative collaboration with scientific and practical institutions, raising methodological standards and increasing consultant assistance to institutions in the area of diagnosing infections, developing new forms of epidemic-control and therapeutic measures, etc.

There is a glorious history to the bacterial production enterprise of the IEM. For many decades, production of bacterials was the most significant aspect of

activity of the institute and those institutions from which it grew and took shape. For a long time, it is expressly the production aspect that determined the image of the institute and its role in the nation--it manufactured a significant part of all products for specific prevention and therapy of infectious diseases, and intensive work was performed to develop new bacterial and viral products and upgrade existing ones.

A special production sector was established when the Central Institute of Epidemiology and Microbiology was founded. As far back as 1938-1939, the institute was in first place in the USSR according to list of high-grade products it manufactured. They consists of sera--antidiphtheria, antidysentery, antitetanus, antigangrene, antibotulinism, antimeningococcal, antiscarlet-fever, antistaphylococcal, antistreptococcal, antipneumococcal, normal; vaccines--typhoid-paratyphoid (mono-, di and trivalent vaccines), combined scarlatina, dry dysentery, typhoid, smallpox; anatoxins--diphtheria and tetanus. In addition the institute produced agents for specific diagnostic reactions.

During the Great Patriotic War, production of agents necessary to assure epidemiological safety of the front and rear was deployed in the organized branches of the Central Institute of Epidemiology and Microbiology--in Alma Ata, Kazan' and Sverdlovsk, and after the end of 1943 again in Moscow, in the department for production of bacterials.

In the postwar years, the Central Institute of Epidemiology and Microbiology produced, as before, large quantities of diverse agents and continued such work after 1945, i.e., after it became part of the USSR Academy of Medical Sciences. By 1965, the institute had developed and set up production of about 80 various biologicals.

At the present time, the enterprise for production of bacterials is concerned with experimental development and production of new agents. There are nine departments in this enterprise: typhus vaccine, BCG vaccine, interferon, staphylococcal anatoxin, diagnostic and therapeutic produces, pyrogenal, fluorescent diagnostic sera, toxoplasmic allergen and antigen, immunodiagnosticum for hepatitis B antigen. In 1976-1980 alone, the enterprise sold various products for a total sum of 1,278,500 rubles.

In 1976-1980, 10 products began to be produced by the IEM: infectious interferon, interferon recovered from cadaver blood leukocytes, immunodiagnosticum for hepatitis B antigen, cow embryo serum, precipitating serum to streptococcus A, monospecific sera against human globulin, antibodies to rabbit γ-globulin, toxoplasmic antigen for immunofluorescence reaction, standard staphylococcal phages (of cattle).

Several of the products developed at the institute (meningococcal, tularemic and brucellar erythrocytic diagnosticums, monospecific sera and lactoferin) have been handed over to other enterprises for production.

At the present time, in the year of its 90th anniversary, the IEM is represented by a monolithic group united by the same main goal, to fight for the health of the Soviet people.

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CSO: 1840/232

UDC 576.85.083.5 : 612.359 + 612.41

GNOTOBIOLOGY AND MORPHOPHYSIOLOGICAL FEATURES OF GNOTOBIOTE ORGANS

Moscow USPEKHI SOVREMENNOY ZIOLOGII in Russian Vol 93, No 2, Mar-Apr 82
pp 287-301

KHLYSTOVA, Z. S., ZAYTSEV, T. I. and PODOPRIGORA, G. I., Scientific Research Laboratory of Experimental Biological Models, USSR Academy of Medical Sciences, Moscow Oblast; Institute of Human Morphology, USSR Academy of Medical Sciences, Moscow

[Abstract] The authors review research with various vertebrates obtained by Caesarean section or decontaminated for studies in immunology, parasitology, space medicine, oncology, pharmacology, physiology, biochemistry, radiobiology and veterinary sciences. Studies have been made of lymphatic systems and the spleen, the blood, the digestive, cardio-vascular, respiratory and endocrine systems and bone marrow. While this branch of biology is new, some conclusions have been reached. Organs that are in direct contact with microflora, e.g., the lymphatic and respiratory systems, the digestive tract and the blood, are generally underdeveloped in gnobiotes, but even those organs with no direct contact, such as the salivary glands, liver, spleen and adrenal glands show histophysiological variations. Increased bile production appears to be tied to increased erythrocyte hemolysis and accumulation of pigments in spleens. Spinal atrophy of the reticular tissue and suppressed lymphopoiesis were also found. Experiments have shown that the latter can be reversed in a normal contaminated environment. Experimental and clinical uses of gnotobiotes require continued research. References 141: 26 Russian, 115 Western.
[226-A-12131]

UDC 616.24-002.022.7:579.882.11]-091-092.9

PATHOMORPHOLOGY OF EXPERIMENTAL ORNITHOSIS PNEUMONIA

Moscow ARKHIV PATOLOGII in Russian Vol 44, No 4, Apr 82
(manuscript received 23 Sep 81) pp 30-37

KUZ'MENKO, V. P., GANDZIY, G. P., BARSHTEYN, Yu. A. and SMOLIY, L. S., Laboratory of Pathomorphology and Pathogenesis of Infection of the Kiev Scientific Research Institute of Epidemiology, Microbiology, and Parasitology

[Abstract] Ultrastructure studies were conducted on the lungs of outbred albino mice experimentally infected with ornithosis. The results showed that ornithosis infection was characterized by multiple foci of inflammation with polymorphic exudate; multiplication of the agent and its invasion of the intercellular space evoked intensive accumulation of leukocytes. The resultant production of toxic products, in combination with extensive phagocytic activity, led to the development of necrotic foci. Extensive overgrowth of connective tissue led to carnificative changes two to three days prior to the onset of clinical symptoms of ornithosis pneumonia. Also evident were various developmental stages of the ornithosis agent within the cytoplasm. Figures 4; references 14: 8 Russian, 2 Ukrainian, 4 Western.
[229-12172]

UDC 616.981.553-036.22-07-08

CLINICAL, EPIDEMIOLOGICAL AND THERAPEUTIC ASPECTS OF BOTULISM

Kiev VRACHEBNOYE DELO in Russian No 4, Apr 82 (manuscript received 10 Mar 81) pp 107-109

SOKOL, A. S., KOLESNIKOV, M. M., ROMAZAN, M. P., KOVBASKO, M. A. and MOROZ, A.S., Chair of Infectious Diseases and Epidemiology, Kiev Medical Institute

[Abstract] A brief survey is presented of the current state of botulism, with emphasis on the fact that 95% of the cases involve home-prepared preserves: 49% of the cases involve meat products (5.4% mortality), 29% involve fish products (27% mortality), and 22% involve plant-products with a mortality rate of 16.1%. Highest mortality figures apply to types E (32%) and A (25%) botulism. A key therapeutic approach consists of gastric lavage with 2% soda solution to eliminate residual toxin, and repeated anema with this solution until peristalsis is restored (usually for 5-6 days). Polyvalent antiserum is administered parenterally and intragastrically, and repeated as indicated by the clinical picture.
[251-12172]

UDC 616.981.51

IMMUNOLOGIC CHANGES IN ANTHRAX IN RELATION TO GENTAMICIN TREATMENT

Tashkent MEDITSINSKIY ZHURNAL UZBEKISTANA in Russian No 3, Mar 82
(manuscript received 29 Jan 81) pp 29-31

AKHMEDOVA, M. D., Uzbek Scientific Research Institute of Epidemiology, Microbiology, and Infectious Diseases

[Abstract] Immune alterations in subjects with cutaneous anthrax or revaccinated with anthrax vaccine and in guinea pigs with experimental infections were investigated for autoantibodies against lymphoid tissues (lymph nodes, spleen). In patients with active cutaneous anthrax, the autoantibodies reached a maximum titer of 1:48 by Boyden's method, and on treatment with antibiotics (streptomycin, penicillin) decreased to 1:10 to 1:15. Low titers (1:16-1:18) were also present in clinically-healthy subjects revaccinated with the anthrax vaccine. Experimental studies with guinea pigs pointed to greatest efficacy of gentamicin when administered at the time of infection; the antibiotic was least effective if treatment was delayed for 24 h. Histologic, ultrastructural, and immunofluorescence studies showed that gentamicin treatment favored recovery of normal histology of the lymphoid tissue in infected animals, and promoted a reduction in anti-lymphoid autoantibodies and in the number of anthrax bacilli found in these tissues. It appears that determination of the autoantibodies in question is of definite value in diagnosing the progress of this infection.
[250-12172]

UDC 616.1: 312.2-06: 612.68(476)

MORTALITY IN CIRCULATORY SYSTEM DISEASES AND ITS EFFECT ON AVERAGE LIFE EXPECTANCY IN POPULATION OF BELORUSSIAN SSR

Minsk ZDRAVOOKHRANENIYE BELORUSSII in Russian No 5, May 82
(manuscript received 15 Apr 81) pp 36-41

TAL'CHUK, A. A., candidate of medical sciences, and MAZURENKO, G. V., Gerontology sector of the Belorussian Academy of Sciences

[Abstract] Using statistics available from the Belorussian Central Statistical Administration for 1969-1970 an analysis was made of the nature of cardiovascular disease among the population of Belorussia, broken down by age-sex and social groups, and computations were made of life expectancy for this population on the hypothesis that cardiovascular disease could be completely eliminated. The results showed the following: cardiovascular disease is the

largest single cause of death; the crude death rate from cardiovascular diseases in this population shows female deaths 1.5 times higher than male deaths (this apparent deviation from male/female ratios is explained by the very large older-female population in Belorussia); the chances of death from cardiovascular disease increase with age; in males, the increased percentage of death from cardiovascular disease starts to climb at age 25 for urban dwellers and at age 30 for rural dwellers; in the 40-44 age groups the chance of death from these diseases is 2.5 higher in males than in females; the highest danger period for females is in the 50-55 age group, associated with the menopause. Tables constructed on the hypothesis that cardiovascular disease is eliminated demonstrate that if this were so life expectancy would increase 5.23 years for females and 4.87 years for men, with members of the urban population gaining more than the rural population. References: 14 Russian
[260-9642]

UDC 616.981.42-036.2(574)

CURRENT PROSPECTS FOR LOWERING INCIDENCE OF BRUCELLOSIS IN KAZAKH SSR

Alma-Ata ZDRAVOOKHRANENIYE KAZAKHSTANA in Russian No 3, Mar 82 pp 7-9

KEREKOVA, B. R., BEKETOV, B. I., KURMANGALIYEVA, A. A. and BARAK, Ts. M., Central Asian Scientific Research Antiplague Institute

[Abstract] Consideration is given to the current prevalence of brucellosis in Kazakhstan and the means being employed to control and eradicate the disease. At the present time approximately 80% of the recorded cases occur in northern and southern Kazakhstan, areas with extensive cattle and sheep farms. Approximately 74-100% of the human cases result from contact with sheep, and the remaining cases are acquired from cattle. The measures that are currently pursued by the public health authorities involve eradication and control of brucellosis in the domestic animals, preventive inoculation of humans at risk of exposure, and early diagnosis by the use of highly sensitive and specific serologic tests.
[260-1172]

UDC 616.981.42-576.8.097.3

CLINICAL MANIFESTATION AND INDICES OF CELLULAR IMMUNITY IN CHILDREN WITH BRUCELLOSIS

Alma-Ata ZDRAVOOKHRANENIYE KAZAKHSTANA in Russian No 3, Mar 82 pp 28-31

NURALINOVA, G. I., Chair of Infectious Diseases, Semipalatinsk Medical Institute

[Abstract] Studies were conducted on the state of cellular immunity and clinical manifestations in children with brucellosis in the Semipalatinsk Oblast, where the incidence of pediatric brucellosis was 22.6% during the last decade. Examination of 215 one-to-14 year olds with brucellosis showed that, in patients less than two years old, the primary manifestations were visceral, whereas the older children presented with joint symptomatology. Chronic conditions were less frequent in the pediatric patients than in adults. Determination of T and B cell levels in the peripheral blood of 50 children showed that cellular immunity (T cells) was depressed in brucellosis; humoral immunity (B cells) was depressed only in patients less than seven years old. During convalescence, B cell levels rapidly returned to normal values, whereas T cell levels were generally depressed for at least a year. References 5: 4 Russian, 1 Western.
[325-12172]

UDC 616.921.5-036.2:576.8.097.3

SERUM ANTIINFLUENZA TITERS IN HEALTHY INDIVIDUALS AS PREDICTORS OF INFLUENZA OUTBREAKS

Alma-Ata ZDRAVOOKHRANENIYE KAZAKHSTANA in Russian No 3, Mar 82 pp 62-63

GALIKEYEV, Kh. L. and ZAVOROKHINA, O. A., Chairoof Microbiology, Semipalatinsk Medical Institute

[Abstract] Serum levels of antibodies against influenza B and A2 were determined by passive hemagglutination inhibition tests in November 1980 in a selected group of clinically-healthy subjects. The results showed that 49.2% of the subjects had moderate (1:40 to 1:80) or high (1:160 to 1:320) titers against influenza B (Leningrad 169/75) virus, while 15.8% had high or moderate titers against influenza A virus. Subsequently, in December 1980, this group experienced an outbreak of influenza B, but not of influenza A. Following the outbreak the percentage of individuals with elevated or high antibody titers against influenza B virus decreased to 22.7%. These observations indicate that an elevation in the percentage of individuals with moderate

or high antibody titers against a given strain of influenza virus may serve as a predictor of an influenza outbreak, and is apparently due to an increased presence of the virus in question in the population at risk. References 5: 4 Russian, 1 Western.
[325-12172]

UDC 612.112.3

LIPOSOME-CELL REACTIONS: LIPOSOMES WITH LIQUID-CRYSTALLINE MEMBRANES

Moscow USPEKHI SOVREMENNOY BIOLOGII in Russian Vol 93, No 2, Mar-Apr 82, pp 214-229

MARGOLIS, L. B. and NEYFAKH, Al. A., Interfaculty Scientific Research Problem Laboratory for Molecular Biology and Bioorganic Chemistry imeni A. N. Belozarskiy, Moscow State University

[Abstract] First used as model membranes in biophysical research, liposomes have been determined to be effective carriers of biologically active substances for timed release to cells. Obtained by various means of introducing phospholipid molecules into a liquid phase, liposomes of such substances as natural or synthetic lecithin can be guided to deliver medications to tumors or other targets. The mechanism of their reaction with cells depends on liposome dimensions, surface charge and cell type, but most importantly on the phase status of the lipid bilayer. Liquid-crystalline phase combinations of about 300 Å can merge with cell walls to release their content, without endocytosis of the liposomes themselves in most cases. Single layer liquid-crystalline liposomes adsorb on cells and their content is diffused into the cells cytoplasm. Many questions remain as to how liposome-cell interaction takes place. Large single-layer liposomes, which adsorb on cells and are absorbed eventually, are relatively less thoroughly researched. References 86: 3 Russian, 83 Western.
[226-A-12131]

UDC 576.858:758.085.23

PENETRATION OF INFLUENZA VIRUS INTO CONTINUOUS LINE CANINE KIDNEY CELL

Leningrad TSITOLOGIYA in Russian Vol 24, No 3, Mar 82
(manuscript received 19 Jan 80) pp 316-319

ANISIMOVA, Ye. A., BUKRINSKAYA, A. G., VONKA, V. and VORKUNOVA, N. K., Department of Viruses, Institute of Sera and Vaccines, CSSR Ministry of Health, Prague; Viral Biosynthesis Laboratory, Institute of Virology, USSR Academy of Medical Sciences, Moscow

[Abstract] Ultrastructural and biochemical studies were conducted on the penetration and uncoating of influenza WSN virus in a continuous line canine kidney cells (MDCK). The virus adsorbs to the cytoplasmic membrane and is also found within phagocytic vacuoles; in both cases the viral envelope fuses with the cell membranes. The data were interpreted to indicate that the virus enters the cell by fusion with the cell wall and also by means of pinocytosis. Since uptake and fusion occurred at 4 and 37°C it appears that non-enzymatic mechanisms are involved. Uncoating appears to involve more than one step since the perinuclear space contained viral (non-spiral) RNP enveloped by the matrix protein. Following loss of the latter protein from the viral core the free RNP enters the nucleus via pores in the nucelar membrane. Figures 6; references 6: 1 Russian, 5 Western.
[242-12172]

UDC 578.085.23:591.044.6

CONTROLLED CELL CULTURE, PART 8: BHK-21 CELL CULTURE ON FLUOROCARBON EMULSION

Leningrad TSITOLOGIYA in Russian Vol 24, No 3, Mar 82
(manuscript received 18 Feb 81) pp 349-351

GAVRILYUK, B. K., LEZHNEV, E. I., MAKAROVA, O. P. and BELOYARTSEV, F. F., Laboratories of Tissue Culture and of Tissue Culture Processes and Apparatus; Institute of Biological Physics, USSR Academy of Sciences, Pushchino

[Abstract] A system was designed and tested for securing three-dimensional culture of BHK-21 cells grown in an emulsion of perfluorodecalin in Eagle's medium. The resultant observations demonstrated that growth on the emulsion (fluorohydrocarbon) droplets became apparent by the third day, and by day 8 a viable cellular film, 1.0-1.2 mm thick, was evident. The high capacity of fluorocarbons for dissolved gases (O_2 and CO_2) appears to render them a suitable support for three-dimensional tissue culture in the case of the BHK-21 cells. Figures 5; references 6: 4 Russian, 2 Western.
[242-12172]

UDC 578.085.23:591.044.6

CONTROLLED CELL CULTURE, PART 9: DYNAMICS OF pH CHANGE IN PERICELLULAR SPACE

Leningrad TSITOLOGIYA in Russian Vol 24, No 3, Mar 82
(manuscript received 1 Dec 80) pp 352-356

AKATOV, V. S., LEZHNEV, E. I., VEKSLER, A. M. and KUBLIK, L. N. Laboratory of Tissue Culture Processes and Apparatus; Laboratory of the Theoretical Aspects of Radiorecovery and Radioprotection, Institute of Biological Physics, USSR Academy of Sciences, Pushchino

[Abstract] Investigations were conducted on the role of pericellular pH in growth cell cultures using Chinese hamster fibrolast cell line (B-11-d-ii-FAF-28 line, strain 431). Sedimentation of cells on an H^+ selective membrane made possible direct measurement of the pH. The results showed that the most pronounced fall in pH in the pericellular space due to accumulation of metabolites occurs within the first six hours of sedimentation or after change of medium. The most significant decrease in the pH, one pH unit, occurs when the cell density in the monolayer is ca. 500,000 cells/cm^2. Consequently, it appears that the decrease in pericellular pH is an important factor in growth limitation and that frequent change of medium favors growth. Figures 5; references 8: 1 Russian, 7 Western.
[242-12172]

EFFECTS OF POLYMYXIN B ON IONIC PERMEABILITY OF BACTERIAL MEMBRANES

Moscow BIOFIZIKA in Russian Vol 26, No 6, Nov-Dec 81
(manuscript received 23 Dec 80) pp 1100-1102

KAPITANOVA, N. G., KOREPANOVA, Ye. A., GARYAYEV, A. A., FROLOV, V. N. and ANTONOV, V. G., 2nd Moscow State Medical Institute imeni N. I. Pirogov

[Abstract] Bactericidal concentrations of polymyxin B were added to susceptible E. coli cells to evaluate the effects on ionic permeability under conditions of aerobiosis and in oxygen-free media in the presence of glucose. Under the latter conditions, K^+ is taken up by the cells and H^+ leaves. Upon addition of K^+ uptake is reversed and the rate of H^+ efflux is decreased. Taking into consideration the effects of this antibiotic bilayer lipid membrane, it appears that the observed effects were due to both an increase in ionic permeability of the bacterial cell membrane and an alteration of the lipid-protein configuration in the membranes. Figures 2; references 9: 3 Russian, 6 Western.
[248-12172]

UDC 576.8-093.3

FURTHER IMPROVEMENTS IN SUBMERGED CULTIVATION OF PLAGUE AGENT AT 37°C

Tashkent MEDITSINSKIY ZHURNAL UZBEKISTANA in Russian No 3, Mar 82
(manuscript received 24 Sep 79) pp 51-53

ORLOV, G. S., Military Medical Service, Turkestan Military Okrug

[Abstract] An analysis was conducted on the factors favoring maximum biomass yield of the plague bacillus in submerged culture at 37°C, using a medium described by others (Ashmarin, I. P., et al., 1975; Orlov, G. S., 1978). The factors which had a positive effect were amino nitrogen, replacement of glucose of galactose, and aeration; prolonged cultivation had a negative effect. The yield of the EB strain approached a maximum of 7.9×10^9 cells/ml under optimum conditions.
[250-12172]

UDC 616.995.121-097

STANDARDIZATION AND STABILIZATION OF BIOLOGICAL PROPERTIES OF ECHINOCOCCUS ANTIGEN

Tashkent MEDITSINSKIY ZHURNAL UZBEKISTANA in Russian No 3, Mar 82
(manuscript received 17 Nov 80) pp 53-55

KURBANOV, A. T. and YUSUPOV, K. A., Uzbek Scientific Research Institute of Medical Parasitology imeni L. M. Isayev

[Abstract] Tests were conducted on methods for the preservation of hydatid fluid for subsequent use in passive hemagglutination tests. The results showed that lyophilized preparations were superior to preparations stored in the freezer of a refrigerator over a period of 19 months in sensitizing sheep erythrocytes and yielding highly sensitive tests. References: 4 Russian.
[250-12172]

UDC: 591.1

BIOELECTRIC FIELDS: THEIR SOURCES, NATURE AND PURPOSE

Moscow USPEKHI SOVREMENNOY BIOLOGII in Russian Vol 93, No 2, Mar-Apr 82 pp 270-286

[Article by V. R. Protasov and O. A. Serdyuk, Institute of Evolutionary Morphology and Ecology of Animals imeni A. N. Severtsov, USSR Academy of Sciences, Moscow]

[Text] The possible mechanisms of effects of weak electric fields on processes of growth, development and regeneration are discussed, as well as the role of these fields on the cellular, tissular, organismic and population levels.

Introduction

Virtually all of the processes in living organisms are related to electrical phenomena. Conformation changes in molecules, ion transport through membranes, movement of unicellular organisms, growth movements of plants, discharge of glandular cell secretions, conduction of impulses in nerve fibers, contraction of muscles, functions of receptors and the extremely complex function of the brain--such is the spectrum, in its general features, of phenomena in which electric fields are involved. It can be stated that electric activity is the inalienable fundamental property of living matter. A comparison of data referable to different branches of physiology, cytology and biophysics gives the impression that the living organism and its environment are, so to speak, permeated with very complex and finely organized, in spatial and time respects, electromagnetic fields, investigation of the parameters and function of which opens up an interesting and multilevel branch of biology [18, 19, 23].

In organisms, currents of charged particles and nonequilibrated electric polarization create static (quasistatic) and variable electric fields within and outside their boundaries. The electric fields of living organisms were named bioelectric fields, although, according to the data of the first researchers--physicists, they did not differ in essence from the physical fields of other sources [62]. Scientists were interested in the bioelectric fields of single cells and entire organisms [53, 71, 85, 88, 90, 98]. However, in view of the intensive development of biochemistry and molecular biology in our times, researchers switched their attention to the chemical aspect of function of living matter, while the physical aspect remained in the shadows in many respects. In the meantime, electrophysiology concentrated on the study of excitable elements [21], while the problem of electric phenomena in unspecialized cells and tissues,

as well as bioelectric fields of whole organisms moved to the background. It is only in the last decades that some serious studies appeared on the role of bioelectric fields in morphogenesis, growth, regeneration and coordination of functions in the organism, as well as on the supraorganismic level--in communication and orientation [28, 30, 74, 97, 103]. We submit here a survey of the main literature on this subject. It should be noted that we shall not deal here with the effects of exogenous electromagnetic (particularly in the radiowave range) and magnetic fields on living organisms (see [20, 28, 37]), as well as some of the links, which are not completely validated, between bioelectric fields and various paranormal phenomena.

The Cell

The thesis that intracellular microfields on the molecular and supramolecular levels are directly involved in processes that occur in living cells has recently gained recognition. Studies are being made of the role of electric fields in self-assembly of biological macromolecules and supramolecular structures [26]. It is known that a difference in potentials appears on mitochondrial membranes during function of the respiratory chain and hydrolysis of ATP, and that a large part of the free energy of metabolism is converted into electric field energy in mitochondrial membranes [5].

Unicellular animals, animal ovicells (mainly fish roe and amphibian eggs), plant spores and pollen are convenient objects for the study of the bioelectric field of an unspecialized cell. The electric fields of an individual cell are recorded by different methods. In particular, the difference in potentials through membranes is measured by means of intracellular microelectrodes; a vibrating electrode is used to examine the electric field in the dielectric environment around a cell, the difference in potentials and specific currents on the surface of tissues are measured by means of low-temperature autoradiography [7].

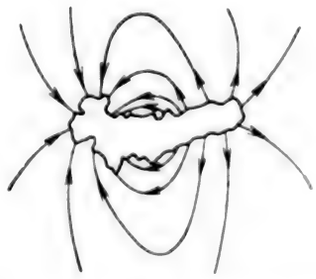


Figure 1.
Distribution of electric current around an ameba [92]

Some of the parameters and time-space characteristics of bioelectric fields of individual cells are listed in Table 1. For the sake of comparison, information is given about the highly specialized electricity-generating cell of the electrical organ of the Electrophorus electricus eel. We see that the electricity-generating cells present no qualitative differences from other cells, although the difference in potentials through the membrane is somewhat higher. For this reason, there are grounds to refer to the general nature of electric potentials of various specialized and unspecialized cells.

As can be seen in Table 1, there is no doubt that there are bioelectric fields (static and pulsed) around animal and plant cells. It is generally considered that the difference in concentrations of different ions is the source of a cell's bioelectric field, which is maintained by means

of active transport through the membrane [46], and the potential-forming cations are monovalent, whereas bivalent ones determine permeability to them of the cytoplasmic membrane. Pulsed electric fields arise as the result of change in membrane permeability and redistribution of ions in accordance with the electrochemical gradient, under the influence of an exogenous or endogenous stimulus. This mechanism has been studied comprehensively in nerve cells and fibers. There are a number of facts that confirm the conclusion that expressly ion current makes a significant contribution to generation of endogenous current and cytoplasmic fields in an unspecialized living cell. In particular, in the ameba, like in the zygote of "pelvetia" [?], incoming static current in the posterior quarter of the body, according to direction of movement, is generated primarily by Ca^{2+} ions, whereas in the growing end of a germinating pollen grain it is generated by K^{+} ions [91, 109]. Experiments with the zygote of Fucus sp. algae revealed that, by the time of the first division, Na^{+} ions enter the future rhizoid end 60% faster, while Ca^{2+} and Cl^{-} enter 10 and 25% slower than into the future thallic end, so that the electric polarization of the cell can be considered as the localization of ion current and permeated regions in different parts of the membrane [76, 77].

Long ago, a link was detected between electric potential of the cell and activity of metabolic processes [87]. At present, it is known that the function of systems of active transport in the membrane to maintain the difference in ion concentrations, which is coordinated with energy expenditure, depends on metabolic activity. Moreover, we cannot rule out the possibility that a specific localization and intensity of electrochemical (including redox) reactions in the cell also affect the appearance of the electric field around it.

Electric phenomena on the phase interface also participate in generating the cell's bioelectric field. Phase interfaces exist in the cell as a result of contact between hydrophobic and hydrophilic structures, mainly lipoprotein membranes and the aqueous phase of the cytoplasmic matrix or extracellular medium. An interphase potential difference should arise on the boundaries of these phases [4]; however, in view of the fact that a stable interphase potential difference is present only on the boundaries of aqueous solutions with dielectric liquids having specific resistance of 10^{16} $\Omega \cdot cm$, while biological membranes have specific resistance of 10^{9} $\Omega \cdot cm$, it can be assumed that the interphase difference in potentials on the cell surface is not large and that it varies markedly, depending on the composition of the medium [58].

Finally, another interesting approach recently appeared to the question of origin of bioelectric field of the cell. Studies of polar properties of its components and the cell as a whole revealed that some proteins, collagen, cell membranes and other structures constitute, by virtue of the orderly arrangement of molecules, electric dipoles, and they can be described as bioelectrets. As we know, electrets are characterized by the presence of a constant dipole moment and fixed electric polarization. Electrets behave like piezoelectrics and pyroelectrics in its direction. It was found that all collagen, keratin and chitins have pyroelectric properties. Pyroelectric properties have been demonstrated in structures of DNA, nucleoproteins, structural proteins of microtubules [39], which play an important part in polar processes of cell division, in preservation of its form during morphogenesis [52, 59]. The

opinion has been advanced that the electret state is a universal property of biopolymers, and that pyroelectric and piezoelectric activity is the basis of physical properties of all living organisms [23, 7, 39, 64]. In this regard, we should mention the hypothesis of origin of life from a complex of crystalline structures [70].

Thus, both electric reactions of the cell and ion voltage through the membrane, as well as phenomena on the phase interfaces and, apparently, other processes, plus other special electret properties of cellular structures--all this together leads to creation of a spatially organized pattern of bioelectric field around a living cell. Let us discuss the hypotheses concerning the purpose of the cell's bioelectric field.

The first, according to Jaffe [74], is related to involvement of the cell's bioelectric field in the mechanism of intracellular localization of growth. According to his hypothesis, the plasma membrane in the future growth region becomes relatively permeable to specific cations. Their movement through the growth region generates incoming electric current. This current, going through the cytoplasm, creates a relatively positive cytoplasmic field under the penetrated segment of membrane. The field causes movement of negative particles toward the penetrated region. This, in turn, increases permeability of the region, and a sort of chain reaction is produced, which is instrumental in localizational growth.

The second, according to Bingley [47], is related to involvement of the cell's bioelectric field in propulsion. Thus, the existence of an intracellular potential gradient in the ameba is related to its propulsive function. As we have already indicated, the ameba generates both pulsed and steady fields. Relatively steady current, with a mean density of 0.1-0.2 $\mu A/cm^2$, enters the posterior quarter of its body and exits at the site of formation of pseudopodia (Figure 1). A reversal of the electric field precedes a change in direction of movement of the ameba [91]. True, the opinion is also held that the change in intracellular potential and change in movement of cytoplasm are different reflections of a more general process [12]. There are also data concerning the link between rhythmic bioelectric phenomena and the beating of flagella and cilia of protozoans, on the one hand, and contraction of their excretory vacuole and the entire cell, on the other [13, 14]. In the opinion of some researchers [72, 104, 105], another mechanism of involvement of bioelectric fields in growth and propulsion is related to local changes in membrane permeability due to their regulation of proton and ion channel function and transport of different ions through the membrane and within the cell [104, 105]. This is particularly important with regard to Ca^{2+} ions, which regulate the functions of contraction and formation of gel in cytoplasmic contractile proteins of the actin and myosin types, which participate because of these functions in cell motility and maintenance of cytoplasmic structure [12, 61]. The latest information about Ca^{2+}-activated actin-microtubule interactions warrants the assumption that contractile proteins are capable of enhancing microtubule-dependent movements.

Table 1. Some parameters of bioelectric fields of some animal and plant cells in the natural environment [first of two parts of table]

Object	Measurement method	Time and spatial characteristics	Current density $\mu A/cm^2$	PD,* mV	Reference
		Animal cells			
Amoeba proteus	Intracellular microelectrode	Process is electropositive (outgoing current at site of formation of pseudopodia)	0.1-0.2	(-40)-(-120) depending on solution	[78, 92]
Paramecium caudatum	Same	Reversed cilia beating associated with depolarization changes in intracellular potential and plasma contraction with hyperpolarization changes	-	-120	[12]
Opalina ranarum	"	Link established between ciliary activity and intracell. potential level	-	(-10)-(-45)	Same
Stentor coeruleus	"	Negative deviations of intracell. potential noted 1.8 s before cellular contraction	-	-30	"
Strongelocentrotus purpuratus sea urchin roe	Extracell. vibrating electrode	Current enters future cleavage groove for 10 min before each division	0.2	-	[74]
Same for Orysias latipes	Same	Current enters animal pole, exits from vegetal pole after fertilization during segregation of cytoplasm	1.0-5.0	-	Same
Same for Xenopus laevis	'	Current enters future cleavage groove and exits from groove within 8 min after start of division	0.5	-	"
Fish melanophore	Intracellular microelectrode	Granule-accumulating end is electropositive	-	(-3)-(+12)	[77, 78]
Rod of rat retina	Intracell, measurement of PD with known resistance	Current enters external segment and exits from internal segment	60.0	-	[74]
Eel's electric organ cell	Intracellular microelectrode	Front side of cell is electronegative	-	120-150	[30]

Table 1 [continued]

Object	Measurement method	Time and spatial characteristics	Current density, $\mu A/cm^2$	PD,* mV	Reference
		Plant cells			
Posterior segment of Acetabularria mediterranea stalk	Extracellular measurement of voltage	Current (pulsed) usually enters growth area	1.0-2.0	-	[74]
Apical filament of Pithophora sp. [Chlorophyceae] green algae	Extracellular measurement of PD on surface	Current enters apical end of cell	-	20	[86]
Ovicell of Fucus sp. [Phaeophyceae] brown algae upon germination after fertilization	Extracellular vibrating electrode	Current enters growing (rhizoid) end	1.0	-	[77, 78]
Growing end of hypha of Neurospora hyphae	Intracellular microelectrode	Growing end is electropositive	-	60	Same
Germinating pollen grain of Lilium longiflorum lily	Extracellular vibrating electrode	Current enters growth area	1.3-10.0	-	[103]

*Here and in Table 2, PD refers to potential difference.

The third hypothesis concerning the purpose of bioelectric fields is related to evolution of electrogenesis [47]. It is assumed that positive potentials of protozoans could be the functional prototype of overshoot action currents of excitable tissue cells. From this point of view, the electric phenomena in protozoans appear to be more general and typical of living cells, as compared to specialized cells of multicellular organisms, and for this reason protozoans can serve as a model in developing universal theory of electrogenesis in living cells [12].

Thus, animal and plant cells are surrounded by steady and pulsed bioelectric fields, the magnitude of which is apparently related to activity of metabolic processes, whereas their spatial configuration is related to localization of ion currents through the membrane and, apparently, electrochemical reactions inside the cell, as well as the orderly structure of living matter (electret properties).

Tissues and Organs (Bioelectric Fields in Intercellular Interactions)

As it has been shown, all cells are surrounded by bioelectric fields. It is easy to imagine that in collections of cells there is interaction between the electric fields of different cells and summation of their energy and amplitude. One of the mathematical approaches to conceptions of such summation has been discussed in [67] on the example of interaction between different action potentials of muscle fibers. It is rather well-known how summation occurs in highly specialized electric organs of some fish, in which individual electricity-generating cells are connected in a specific order [3, 30]. We should add to this that the intercellular substance, which has an orderly structure, is also instrumental in maintaining electric polarity of tissues. Most supporting tissues of vertebrates demonstrate marked electret properties, due to the presence of collagen in the intercellular space [38, 83]. All this also applies to the tissues of invertebrates and plants [101].

On the tissular level, bioelectric fields are involved in intercellular interactions, and we can distinguish two components in their action: force (migration of charged particles) and information. We shall discuss them in greater detail.

In recent times, many researchers believe that bioelectric fields are involved in morphogenesis and regeneration. Both of these processes are phenomena of the same order, since they are related to reproduction, growth and differentiation of cells. It has been long known that bioelectric fields are somehow related to morphogenesis [86]. There are many hypotheses concerning the mechanism of morphogenesis in embryology. Various models (embryonic fields, positional information [74, 103]; phase shift, "sand" model [84] and others) have tried to explain how linear genetic information is translated into a distinctly organized three-dimensional spatial structure and what factors affect cell differentiation. Embryologists often use terms such as field, pattern and gradient, imparting a purely morphological meaning to them and without relating them to physical fields. The concept of field was first introduced to biology by Gurvich as far back as the 1920's [11]. Without defining the physical essence of a biological field, he attributed to it the role of a factor that

organizes living matter in time and space, in morphogenetic processes. However, an increasing number of studies is indicative of the physical (more precisely, electric) nature of these fields and confirms hypotheses expounded previously. The idea has been discussed that, by virtue of vector properties, a bioelectric field constitutes a matrix, within which genetic information is expressed [40, 54].

The influence of exogenous, artificial and very weak static electric fields on morphogenesis and regeneration is direct evidence of involvement of bioelectric fields in morphogenetic processes. As far back as the 1920's, Lund [86] published a series of interesting articles on regeneration of the Coelenterata, Obelia, in a static electric field. He discovered that during regeneration in an electric field with current density of 0.02 mA/mm^2, the hydranth always grows with the front (top) end toward the anode, regardless of orientation of the regenerating object. It was demonstrated that the direction of differentiation during regeneration can be reversed by superposing an exogenous electric field close in magnitude, but in the opposite direction, to the object's own field. The author concluded that electric polarity is primary in relation to morphological polarity, and that the mechanism determining the morphological polarity can be controlled by means of an exogenous electric field. Rose [95-97] confirms these data in several current works with Coelenterata, and he goes even farther. He demonstrates that a change in polarity of an organism is always related to a change in direction of the bioelectric field, that the region with maximum metabolic activity always becomes the center of organization and that this center is electronegative in relation to other regions. Rose advances a hypothesis concerning the mechanism of effect of the bioelectric field on differentiation (see below).

There is also a series of studies dealing with regeneration of Planaria worms [57, 87]. Planaria without head and tail segments were immobilized in gel and placed in a weak, steady electric field. Under specific conditions of current density, the head structures always grew at the cathode, regardless of the animal's orientation. Planaria with two head segments were obtained in this manner [57].

A link between wound regeneration and healing, on the one hand, and electric phenomena, on the other, was also demonstrated in vertebrates. It was shown that the electric characteristics after amputation of a limb were different in regenerative and nonregenerative amphibians [41]. Other studies demonstrated that one can accelerate regeneration of a triton limb by means of an artificial electric field [58, 100]. Moreover, a vibrating electrode was used to measure and map the natural electric fields around the stump of an amputated triton limb. It was shown that elimination of Na^+-dependent current in the stump, by means of blocking the Na^+ channels of membranes with amiloride or removal of Na^+ from the medium stopped almost entirely or severely retarded regeneration [48, 49]. There are also data concerning electric stimulation and partial regeneration of mammalian limbs also [43]. All this warrants the belief that endogenous electric currents and fields are essential to normal regeneration.

Many works have been published about the effects of endogenous and exogenous electric and electromagnetic fields on fusion of bone fractures (see [51, 60]).

Clinically noticeable healing can be induced with 10 μA current. New bone tissue is formed in the immediate vicinity of the implanted cathode. The opinion is held that, in this case, it is not the field, but electrode products that produce the effect, but there are also other facts, according to which an exogenous electromagnetic field stimulates fusion of fractures [56, 106]. In this case, the effect of electrode products is ruled out. It is known that direct current of 200 μA accelerates healing of skin wounds in rats, even if it is used for the first 4 h after the wound was sustained. It is believed [69] that electric current influences cell migration, but not proliferation.

Direct electric current accelerates healing of injuries in plants. A comparison of the data shows that there is a similarity of optimum level (μA) and polarity (cathode demonstrates healing action) in plants and animals, although optimum current density is lower in plants [66].

Thus, we see that electric fields are involved in some way in processes of migration, growth and differentiation of cells and tissues. What is the mechanism of this involvement? There are several hypotheses on this score at the present time. All of them are expounded on the basis of the fact that bioelectric fields of individual cells create special electric conditions in the intercellular space. One of the assumptions is that the electric field creates guided transport of specific repressors, thereby providing for the appropriate pattern of cell differentiation [95]. This has been confirmed by experiments. For example, if two identical segments of the stalk of the Coelenterata, Tubularia, are successively connected, the top one always continues to grow and forms the upper structures (tentacle [palp], hypostoma) of the hydranth, while the lower one stops growing. As a result, from the two segments, each of which could have developed into a whole hydranth, only one normally formed organism develops. If, however, similar segments are connected "face to face," both will regenerate as if there were no interaction between them, and each will develop into a whole hydranth. In other words, the repression that occurred in the experiment from the top segment to the bottom one was not manifested in this case. This can be evaluated as evidence of directionality of repressor currents. The fact that this repressor current generates a bioelectric field is proven by other experiments, which deal with the effects of weak exogenous electric fields on regeneration of hydranths, as well as the presence of a difference in potentials at the ends of the stalk [96, 97, 100]. However, if this is so, all repressors should have a charge of the same sign and similar magnitude, which is unlikely. For this reason, even if this hypothesis is valid, it is so only for lower organisms with rather simple structure of bioelectric field. In plants, in particular, the role of bioelectric fields in phytohormone transport cannot be ruled out.

Jaffe [73] proposed the following model: the bioelectric field does not move repressors, but charged components on the plasma membranes of cells. He called this phenomenon lateral electrophoresis, and he proved mathematically that it is possible for charged membrane components to be redistributed under the influence of endogenous or exogenous electric fields with a drop of only a few millivolts in potential through the cell. The equiponderant concentration of identical negative particles or molecules on the surface of a spherical cell placed in a homogeneous field, when there is equilibrium between

electrophoresis and reverse diffusion, constitutes $C = \overline{C}(\varepsilon \cdot \mathrm{csch}(\varepsilon)]e^{\varepsilon \cos\theta}$, where $\overline{C}$ is mean concentration of particles, $\varepsilon = (m/D) \cdot (\overline{V}/2)$, m is electrophoretic mobility, D is diffusion constant, $\overline{V}$ is potential difference through sphere in a given electric field. From this equation, one finds that $\overline{V}_{0.1} = 0.6\ (D/m)$, i.e., one can, by taking into consideration electrophoretic mobility of particles and their diffusion constant, determine the required voltage to induce 10% polarization. Inserting in the equation the mean values for biological spherical particles 10 nm in diameter, Jaffe estimated that, for 10-50% polarization, prolonged constant decline of potential through the cell of only 0.8-40 mV will be required. According to the data in Table 2, an endogenous potential difference sufficient for electrophoresis along cell membranes is widely distributed in tissues of living organisms.

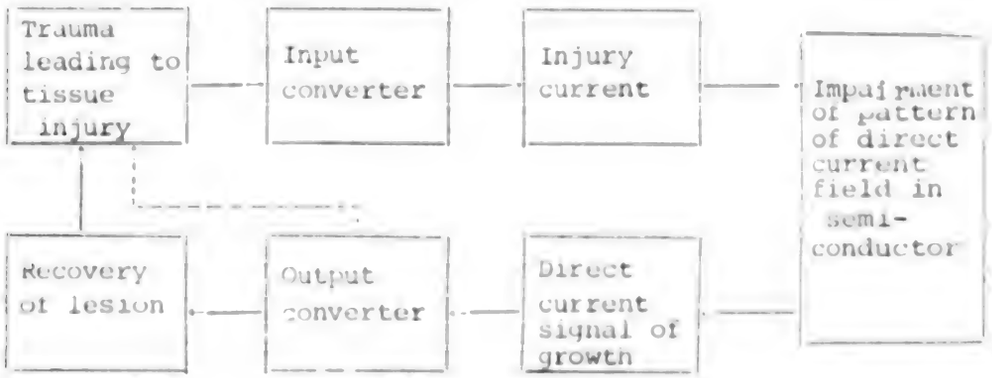
Table 2. Some characteristics of bioelectric fields of animal and plant organs and tissues

Object	Spatial characteristics	PD, mV	Source
	Animals		
Obelia			
stalk segment	Top end electronegative in relation to bottom one	1.0-1.5	[98]
trunk wall	Same	(-1.0)-3.0	[87]
Anodonta sp., epithelium (mantle)	Outside electronegative in relation to inside	18.5	[86]
Fundulus sp., gastrula	Same	(-7)-(+1)	[74]
Chick, chorioallantois	"	-3	Same
Rabbit, blastomere wall	"	-7.8±0.6	"
Ambustoma tigrinus, regenerating tip of paw	Current exits from regenerated end of paw, enters proximal to it	Current density, 30-100 mA/cm^2	[49]
deformed bone	Bent-in side is electronegative	-	[6]
	Plants		
Oats, coleoptile	Current flow up in outside cell layer and down in inside one	20-80	[86]
Onion, root	Region of highest potential corresponds to region of maximum mitotic activity	20	Same

Experiments with electrophoresis along the cell membranes of Concanavalin A receptors, as well as acetylcholine receptors, serve as convincing evidence of the validity of Jaffe's hypothesis [94, 95]. It was demonstrated that an electric field of 4 V/cm causes significant redistribution of Concanavalin A receptors along the plasma membranes of mouse embryo cells in 4 h. The receptors (apparently, glycoproteins) are concentrated on the cell side facing the cathode, in accordance with the mechanism of passive electrophoresis. The

fact that this is a passive process is proven by experiments involving the use of metabolic inhibitors [94]. Jaffe believes that lateral electrophoresis is one of the most important mechanisms, upon which are based the effects of endogenous fields in developing systems, including determination of direction of growth in plant meristems, nerve cell growth, development of embryonic tissues, etc. He believes that the same mechanism is involved in processes of limb regeneration in vertebrates. Thus, in a steady electric field, the growth of axons is accelerated in the direction of the cathode as a result of lateral electrophoresis [75]. It is also known that when current exits from the end of a stump (which corresponds to natural distribution of endogenous current), a large amount of nerve tissue is formed and regeneration proceeds normally. If, however, there is incoming current (against natural currents), there is a decrease in amount of nerve tissue and degeneration occurs. Bodemer [74] obtained some regeneration of the limb of an adult frog by stimulating the nerve in the scapular region at the rate of 1000 pulses/s, with amplitude of 300 MV for 1-2 min. On the basis of the fact that the denervated limb did not regenerate, it was concluded that the nerve is somehow involved in transmission of morphogenetic information. The possibility cannot be ruled out that, by creating a field around itself, it becomes an important element of the mechanism that controls regeneration. At any rate, it is believed that nervous processes in the stump are the target of endogenous and exogenous fields. Hence, the possible influence of weak incoming endogenous current on regeneration consists of accelerating growth of nerve tissue by means of lateral electrophoresis. Then the nerve tissue, generating a specific electric field, is instrumental in morphogenetic and growth processes.

Becker uses a unique approach to questions of healing and regeneration [40, 42]. Proceeding from the conception of initial biologically solid state, he believes that signals about trauma are transmitted by a flux of electrons within the matrix, which leads to a change in pattern of the system's electric field and ultimately to regeneration (see chart).



This chart is applicable to recovery from bone tissue injuries. The mechanism of effects of an endogenous electric field is more or less known. It is based on the electret properties of bone. As a result of damage to osseous tissue, by virtue of its piezoelectric properties, the appearing electric field is

instrumental in producing orderly orientation of macromolecules synthesized by cells, which participate in healing. Exogenous artificial electric fields have a similar effect, and they accelerate bone fusion [56, 63, 106]. However, this mechanism is not flawless. It has been estimated that fields of 300-3000 V/cm are required for individual elongated biological particles oriented at an angle to the direction of voltage; for example, 4000 V/cm is required for collagen molecules 0.9 μm in length and 50 V/cm for only actin filaments 1-10 μm in length [74]. These figures are 100 or more times higher than the known levels of electric field intensity within tissues, so that some researchers consider this mechanism unlikely. But, it is quite possible that, in this case, it is not passive electrophoresis, but some other (active!) mechanism that is involved in orientation of polar molecules in a bioelectric field.

Athenstaedt [38, 39] believes that such a mechanism, which is based on electret properties of living matter, determines not only growth of osseous tissue, but morphogenesis and growth as a whole. He writes that growth of animal and plant structures always proceeds in the direction of the positive pole of the existing longitudinal electric polarization. This applies to collagen, keratin, chitin and plant structures. Evidently, as growth progresses, the polar linear macromolecules are so oriented that the positive pole of their constant dipole moment always points to the direction of growth. The chorda, neural tube and bilateral row of somites constitute the axial system of the chordate embryo. It was found that the direction of longitudinal electric polarization is the same in all vertebrate embryos examined: minus is cranially located and plus caudally. From this, the author derives a "physical matrix" of the chordate embryonic axis system.

Let us consider another hypothesis. It is concerned with the possible involvement of bioelectric fields in establishing and function of intercellular contacts. This applies mainly to embryonic development of organisms. These facts are known: cell reproduction is radial if a tissue explant is cultivated in the appropriate medium. With simultaneous cultivation of two explants side-by-side, radial reproduction of cells proceeds along the lines that connect the pieces of tissue, and orientation of cells regresses with the square of the distance between explants [80]. It was found that growth is suppressed after establishment of intercellular contacts along the axis that connects the pieces of tissue. All this indicates that there are interacting physical fields around the explants, which determine the direction of cell growth and spatial position of intercellular contacts [81]. Experiments with reorientation of cell growth by applying an exogenous electric field prove that these fields are electrical [80]. These facts have a direct bearing on problems of morphogenesis, since processes of establishment of cell contacts, linkage of cells and, accordingly, structural shifts and morphogenetic movement of cell masses in building the organism depend on the electric potential of cells.

Brick et al. [50] submit an equation, according to which an increase in the cells' surface potential intensifies repulsion of cells and raises the energy barrier, which serves to link cells and establish contact between them. The differences in electric field characteristics of various cell populations and change in this parameter within a population may consist of change in

degree of linkage and contact between cells and, consequently, displacement of cells during development. An experiment on developing frog eggs revealed that the transition from blastula to gastrula is related to change in electric potential on the cell surface; in turn, this is related to shifts in the epithelium: cells that remained motionless during the period studied showed no change in potential. Interestingly enough, the enloderm is always more negative than the chordoderm, which is more negative than the internal nervous ectoderm. This hierarchy is maintained throughout gastrulation. In other words, there is a change in degree of tissular linkage by means of electric fields of cells [42]. This phenomenon is known for embryonic cells [44]. Coordination in cell tissues is effected, apparently mainly due to the presence of special electrotonic fissural contacts [45]. Fissure contacts are not retained upon cell division, and with tissular growth there are new fissure contacts, and it is quite likely that their location is determined by the tissue's electric field.

With reference to the question of electrotonic coordination [conjugation], we should mention one more possible function of bioelectric fields in organisms. Electrotonic coordination by means of fissure contacts is related to supracellular integration of conduction, which perhaps occurs independently of neuromediatory systems. The special spatial location of fissure contacts warrants the assumption that they form a morphologically distinct network, which serves for nerve-free transmission of information in the organism. This applies not only to the embryonic stage of development, but adult specimens, at least on the prenerve levels of organization (sea gooseberries [Ctenophora], siphonophores, Coelenterata). It is theorized that such a system persisted in higher organisms [25]. In modern animals, there are two systems of electric transmission of information: a specialized high-speed nervous system for transmission of action potentials and another, primitive one, which perhaps preceded the first one. The existence of this system has some bearing on the problem of acupuncture [25, 42]. In general, it is assumed that the system of electrotonic connections in organisms serves as the structural basis for the function of bioelectric fields, which synchronize and integrate the function of individual cells, tissues and organs.

Speaking of the role of bioelectric fields in electrotonic transmission of information, we should mention studies of ephaptic phenomena in central nervous system synapses. They refer to the fact that interactions between neurons and fibers may be effected not only chemically, but by means of endogenous electric fields [35]. Involvement of ephaptic interactions is observed in synchronizing activity of a large number of nerve cells. Moreover, such mechanisms can both excite and inhibit neuronal impulsation activity. Their role is also being studied in the passage of nervous excitation to an effector organ, in particular a muscle.

Finally, many works dealing with physiology of plants indicate that their bioelectric fields may be involved in transport of phytohormones, coordination of physiological growth processes and plant reactions to changes in environmental parameters (see, for example, [24, 65, 86]).

Thus, the endogenous bioelectric fields of tissues and organs, which appear as the result of summation of electric fields of individual cells that make them up,

are perhaps involved at the early stages of ontogenesis in processes of morphogenesis and growth, regeneration and healing, nerve-free transmission of information within the organism, coordinating its internal processes. Some researchers believe that it is expressly on this basis that highly specialized functions of the nervous system could develop for transmission of information and coordination of organ function in multicellular organisms. In the absence of a nervous system or when it is poorly developed (in lower animals, plants, at early stages of ontogenesis), these functions may be effected by bioelectric fields of unspecialized cells and tissues.

Bioelectric Field Around Organisms

At the present time, there is no question about the existence of low-frequency electromagnetic fields around living organisms, due to their bioelectric activity. It should be noted that the magnitude and spatial configuration of an electric field around an organism depend on the conduction properties of the environment; for this reason the bioelectric fields of animals living in water, which has electroconductive properties, differ (quantitatively, qualitatively, as well as in significance to vital functions) from the electric fields of terrestrial organisms. The capacity to orient themselves in weak electric fields is indicative of the major role of electricity in the life of marine organisms. Protozoans, some mollusks, crustaceans and worms have this capacity. But bioelectric fields play a particularly important part in the life of fish. Already in antiquity, it was known that some fish are capable of "hypnotizing" at a distance and striking their prey. However, it is only in the 18th century that these phenomena were identified as electrical. For a long time, the purpose of electric organs of so-called mildly electric fish was not comprehended. It is only in 1958 that Lissman (see [30]), who used the latest electronic technology, established that these fish use their electric fields for orientation and communication.

Each discharge of electric organs in water generates a typical electric field around the fish (Figure 2). Its structure depends on the shape of electric organs, location and orientation of electric plates in them, as well as location of electric organs in the body and shape of the body.

Specialized electricity-generating cells of electric fish originated from muscle (most species), nerve (in some electric eels) or glandular (electric catfish) cells. High-tension (in freshwater strongly electric fish) or high-power (in saltwater fish) currents appear as the result of summation of potentials of individual electric cells, which are interconnected in series and parallel. Appearance of large exogenous electric fields upon synchronous function of nonspecialized neuromuscular tissues (Table 3) was discovered [30] in some nonelectric fish (Uranoscopus scaber). In some fish, perception of electric fields occurs by means of specialized electroreceptors or (in their absence) directly by neuromuscular structures or receptors intended for perception of nonelectric stimuli. The following chart illustrates the significance of bioelectric fields of fish [on the next page].

We should dwell in particular on the possibility that fish use their bioelectric fields in shoal behavior. It was established that there is summation of bioelectric fields of individual specimens in excited moving shoals of fish [31,

32]. There is summation of energy and amplitude, with formation of a single electric field of the shoal, which apparently assures the simultaneousness of maneuvers of all specimens in the shoal. The opinion is held [30] that the overall electric field of a shoal is used by fish for navigation purposes, by means of interaction of fish shoal currents with the geomagnetic field.

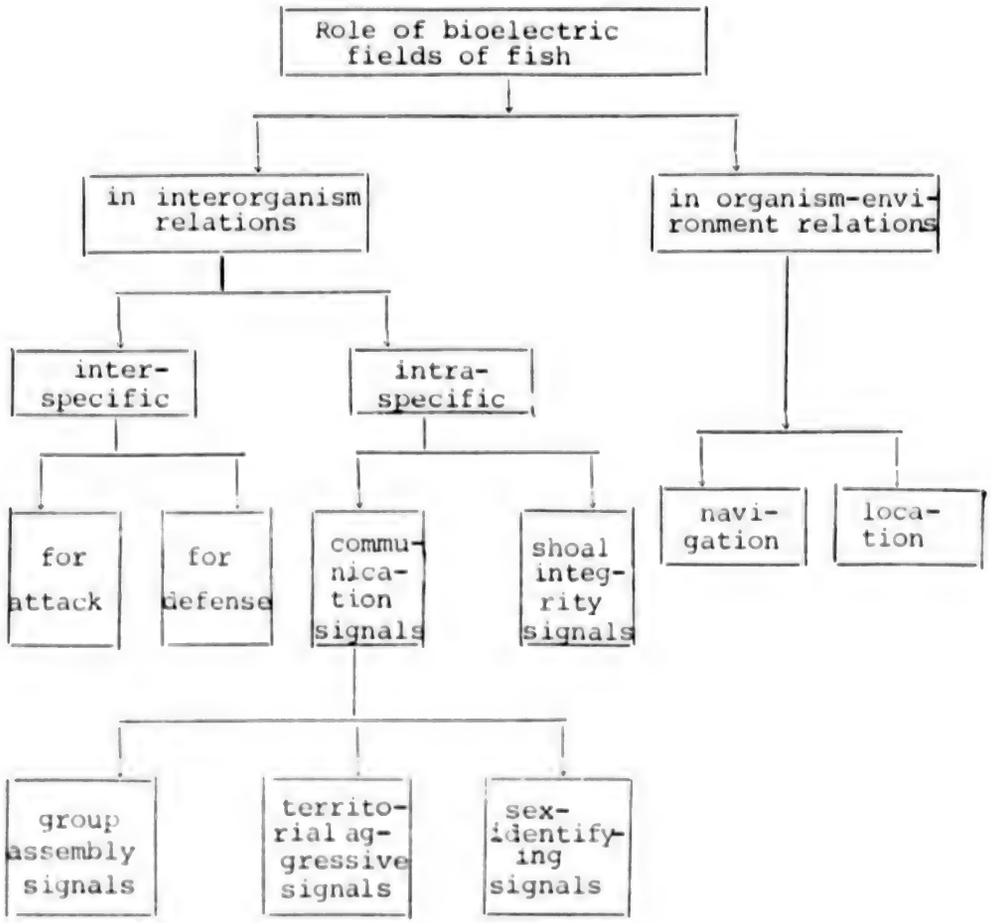


Table 3. Some electric characteristics of fish

Species	v, V	I, A	R,	P, W
Electric eel, Electrophorus electricus	800 (to 1200)	1	600	10^3
Torpedo ray, Torpedo marmarata	60	50	1	10^3
Weevil, Gnathonemus petersii	4	10^{-3}	1000	10^{-2}
Loach, Misgurnus fossilis	10^{-4}	10^{-7}	100	10^{-11}

Key: v) voltage over length of fish
I) current in water
R) resistance of water
P) power of generator

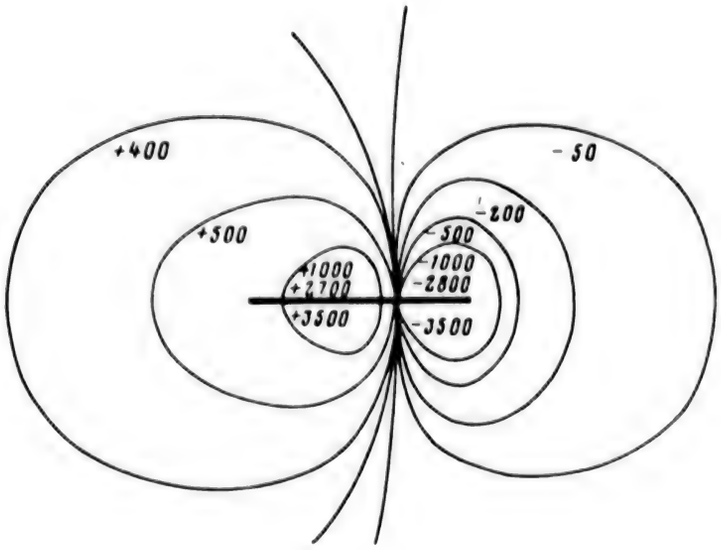


Figure 2. Electric field of dipole type currents in fish (boldface line, tail on the right) [70]. The numbers refer to equipotential lines (mV)

In the course of evolution, fish developed the capacity to use their bioelectric fields in various areas of their activity, and evolution of different systematic groups in this direction proceeded independently (in parallel), which is indicative of the possibility of development of similar morphofunctional distinctions in virtually all representatives of the fish class.

In general, we cannot deny the possible role of bioelectric fields on the supraorganismic level in other aquatic organisms, rather than only in fish, for orientation (navigation) and maintaining communications between specimens in communities and shoals [herds].

A bioelectric field was first discovered in the air environment in 1949, at distances of up to several millimeters around the frog's sciatic nerve [55]. Later, it was recorded in experiments on frog muscles and the human forearm with a special antenna at a distance of 1 cm. Gulyayev obtained the best results with remote [without contact] registration of biopotentials [8, 19]. Modern equipment permits demonstration of an electric field at a distance of several meters away from man.

It is believed that the overall electric field of terrestrial organisms consists of at least two parts: electrotonic, which is related to activity of individual organs, and triboelectric, which is due to mechanical movement of parts of the body carrying a superficial electric charge [7, 34]. Electric activity of the muscular and nervous system (chiefly the heart, muscles, brain) makes a particularly large contribution to generation of the overall bioelectric field around an organism, to a lesser extent blood flow [2] and secretory organs

[33] are implicated. With regard to the triboelectric component, it should be noted that generation of an electric field in, for example, bees is related to the capacity of chitin integuments to carry a relatively high electrostatic charge [17]. This also applies to animals with well-developed pelage.

The question of the role of bioelectric fields surrounding terrestrial organisms is still debatable. Theoretically, by analogy to aquatic animals, it can be assumed that the fields have some involvement in organism-environment and organism-organism relations. It is considered quite possible that exogenous electromagnetic fields can affect the organism via its bioelectric fields [1, 15, 16, 27-29]. Some researchers [28, 36] tend to attribute such, seemingly, diverse phenomena as changes in incidence of traffic accidents, mental illness, harvest, etc. to the link between the organism and changes in environmental electromagnetic fields [36, 54, 78]. On the basis of a large amount of facts, it can be concluded that bioelectric fields are an objective reality, an inalienable feature of all that lives. Moreover, electric activity of cells and tissues has been used more than once in evolution of different systems. High-speed conduction of electric impulses was able to develop on its basis; an entire group of fish developed the amazing capacity to generate and perceive strong electric fields and use them in different areas of their activity. We can assume that bioelectric fields are involved in processes of morphogenesis, growth and regeneration, as well as nerveless transmission of information within multicellular organisms.

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EFFECT OF LOCAL VIBRATION ON DIVERS WORKING UNDER WATER

Moscow GIGIYENA TRUDA I PROFESSIONAL'NYYE ZABOLEVANIYA in Russian No 11, Nov 81 (manuscript received 16 Oct 81) pp 32-35

[Article by A. V. Sterlikov, F. P. Lakhov, V. V. Ivanov and A. K. Belukhin (Moscow), Institute of Water Transport Hygiene]

[Text] In our country, construction of underwater gas and oil lines, dams and moorage, which involves considerable work by divers working in ventilated gear, is proceeding at a rapid pace. Pick-hammers, pneumatic drills and other vibrating tools are used often in underwater work. Divers make use mainly of low-frequency vibrating tools, whose oscillations constitute a frequency of 10-16 Hz.

The conditions under which man is exposed to local vibration under water are very different from those on the ground, due to the presence of a number of aggravating factors: cooling of the working limb and entire body, elevation of partial oxygen tension, compression and intensive noise. For this reason, it is necessary to work out the hygienic specifications for the diver's work tool according to level of vibration it generates.

Our objective here was to study the effect of local vibration generated by a tool on a diver during work, determination of physiological changes and dynamics of recovery thereof.

The studies were conducted on 11 professionally trained divers, who were allowed to perform underwater work on the basis of their physical condition. They ranged in age from 24 to 36 years, and their qualifications were rated as second and third class. The divers worked in ventilated gear and they had not previously used vibrating tools. The study was conducted in a tank at a depth of 5 m, in which a special support was installed for the vibrating tool. Water temperature ranged from 16 to 20°C, air from 22 to 28°C during the experiments.

For work under water, a type S-358 pneumatic concrete breaker, designed to break up reinforced concrete, excavate rocks and dig trenches was used. Operating pressure of the tool constitutes 6 kgf/cm^2, it weighs 18 kg and fundamental frequency of vibration is 13 Hz. Overall vibrating rate of the tool constituted 130 dB, with prevalence at low frequencies of 8 and 16 Hz and 123 and 124 dB, respectively.

We conducted four series of experiments. In all series, the divers worked under water for 2 h (maximum time according to GOST 12.3.012-77 "System of Standards for Labor Safety. Work of Divers. General Safety Requirements"), divided into 15-min segments with 5-min rest periods.

The first was a control series, and the divers worked in the same position as with a tool, but without delivery of air. In the second series, the subjects worked with the tool whose vibrating rate constituted 105 dB. In the third series, the vibrating rate of the tool was 120 dB and in the fourth 135 dB.

The procedure for training and examining the divers before submerging and after getting out of the water was as follows: at first, we conducted "background" observations before work, which included examination by an otolaryngologist, measurement of sensitivity to vibration (using an IVCh-2 instrument), rheography of the right arm using a 4-RG-1A rheographic attachment and Elcar electrocardiograph, measurement of sublingual temperature and arm temperature (TEMP-1 electric thermometer), determination of maximum strength of right and left hands and static muscular endurance by means of a liquid dynamometer.

After the diver's ascent, which took 4 min, we determined sensitivity to vibration in the 5th min, then 10, 30, 60, 90 and 120 min later. Concurrently we performed rheography of the right arm. Ten min after getting out of the water we measured sublingual temperature and temperature of the skin of the right arm, and after 30 min, after the diver's gear was taken off, we measured muscular strength and static muscular endurance.

The methods of examination were selected in accordance with the "Methodological Recommendations for Setting up Differentiated Standards for Local Vibration," approved by the USSR Ministry of Health.

The Table lists the estimates of sensitivity to vibration, maximum strength and static endurance.

Dynamics of changes in sensitivity to vibration of divers working under water (M±m, n = 11)

Series	Vibration frequency, Hz					
	16	32	63	125	250	500
1 (control)						
Base data	15.0±3.87	15.7±4.38	1.6±4.09	3.1±2.89	5.8±3.62	10.0±5.92
4 min after work	22.4±3.28	22.0±4.77	14.7±7.61	24.7±3.87	35.7±6.53	33.6±6.71
60 " " "	16.6±4.21	15.3±3.97	4.1±1.65	4.8±1.62	6.2±2.09	9.43±3.14
90 " " "	14.4±4.25	15.2±4.16	16.8±3.76	4.5±2.88	6.6±3.16	10.8±4.9
2--105 dB						
Base data	14.0±2.47	13.2±4.2	0.4±2.55	2.7±2.45	0.2±1.85	1.9±3.59
4 " " "	22.5±2.54	22.0±3.46	15.3±4.34	20.7±3.88	22.6±6.8	25.0±5.42
60 " " "	15.4±3.81	15.3±3.9	4.9±5.07	7.9±3.47	6.7±3.88	7.3±3.35
90 " " "	13.6±2.38	13.0±4.16	0.5±2.54	2.40±2.16	0.4±1.63	1.7±3.55
3--120 dB						
Base data	16.2±3.27	15.0±4.27	4.6±4.72	8.0±2.35	9.4±5.22	11.0±5.72
4 " " "	24.1±2.96	24.6±3.32	20.1±3.82	28.8±6.74	31.8±7.77	33.8±5.73
60 " " "	18.5±3.61	18.5±5.27	8.7±6.76	15.4±7.2	17.7±7.29	22.2±10.1
90 " " "	16.2±3.46	15.2±6.69	6.0±6.42	10.2±4.77	12.4±7.23	16.5±10.1
120 " " "	16.1±3.22	14.4±6.5	5.1±4.96	7.7±3.23	9.2±6.42	11.0±5.22
4--135 dB						
Base data	12.7±3.66	12.1±3.74	0.3±4.93	3.1±3.87	9.6±3.26	2.3±4.48
4 " " "	24.1±2.96	23.3±3.32	16.6±4.23	23.3±4.01	23.9±4.83	26.5±5.52
60 " " "	16.9±1.22	16.4±2.58	7.4±3.11	10.0±3.44	9.0±3.81	10.0±5.19
90 " " "	15.6±1.43	15.0±2.76	4.2±3.26	6.8±3.41	5.6±2.91	5.9±4.09
120 " " "	13.8±2.75	12.7±3.23	1.7±3.72	4.9±3.33	2.3±3.21	3.4±4.11
135 " " "	12.4±3.64	12.0±3.79	0.4±4.13	3.0±3.69	0.4±2.81	1.9±4.01

In all cases, the rheographic index presented changes in different directions, so that it could not be used to determine the nature of changes in blood flow rate in arm vessels of divers after work, and for this reason this parameter is not discussed hereafter.

We observed an increase in sensitivity to vibration after the subjects had spent time under water. It was the most marked at high frequencies, regardless of level of vibration. At low frequencies (16 and 32 Hz) the temporary shift of thresholds of sensitivity to vibration progressively increased with increase in vibration level.

Time of recovery of vibrosensitivity increased with increase in vibration level. Thus, at frequencies of 16 and 32 Hz, vibrosensitivity was restored after 60, 90, 120 and 135 min in the four series of experiments.

Maximum muscular strength and static endurance diminished during exposure to vibration. Body temperature dropped by 0.9-2.4°C and skin temperature of the arm by 2.7-4.6°C during submersion, in all series of experiments.

In the fourth series of experiments, the subjects complained of pain in the hands, cooling of the wrists and arm, as well as paresthesia. These signs disappeared 3-4 h after terminating the work.

The effect of local vibration on the diver is combined with a number of factors, which enhance the physiological changes it elicits. These factors include local and general cooling, static tension due to the contrived position. Synergism of these factors with regard to local vibration has been well-proven for conditions on land (N. N. Malinskaya; M. F. Stoma).

Moreover, such specific factors of underwater conditions as elevation of oxygen pressure and compression may also enhance the adverse effect of vibration on man when working under water. Breathing a gas mixture with high partial oxygen pressure itself leads to a decrease in blood flow and development of capillary spasm (G. L. Zal'tsman et al.); apparently it should increase capillary spasm elicited by local vibration. As a result of compression, blood is driven from vessels of the hands, particularly capillaries. This worsens tissular circulation, increases the cooling effect of water and, apparently, alleviates development of capillary spasm as a result of vibration.

The combined effect of the above-mentioned factors could be so strong that the changes in physiological parameters they elicit become capable of obscuring the effect of vibration proper. Thus, in the control series of experiments, during which the divers merely submerged and were not exposed to vibration, they presented marked decrease in vibrosensitivity at high frequencies (63 Hz or more) and less marked decrease at low frequencies (16 and 23 Hz). However, it was the same at high frequencies as after 2 h of exposure to vibration with intensity of 105-135 dB, whereas at frequencies of 16 and 32 Hz we observed progressive increase in temporary shift of thresholds of vibrosensitivity with increase in vibration level. Thus, at frequencies above 32 Hz, vibrosensitivity was not an informative parameter, with regard to quantitative characteristics of local vibration generated under water by a pick-hammer. Moreover, this could

be due to the fact that the maximum energy of vibration in the concrete breaker used in the described experiments was concentrated at low frequencies (16 and 32 Hz).

We selected the changes in parameters of vibrosensitivity at low frequencies, which are observed on the ground at the end of a work day in individuals working with vibrating tools (A. M. Mikul'skiy; Z. M. Butkovskaya et al., and others) as criteria of permissible effects of local vibration on divers after diving for the maximum permissible time (2 h) and the criteria of permissible changes in maximum muscular strength and static endurance according to the "Methodological Recommendations for Setting Differentiated Standards for Local Vibration With Consideration of Vibration Force Characteristics."

A comparison of the results of our experiments to the above-mentioned criteria revealed that at up to 120 dB levels of vibration the changes caused by it can be considered permissible, since they do not exceed the ranges designated by the chosen criteria. The only exception was a somewhat longer time of recovery of vibrosensitivity after work. If, however, the vibration level exceeded 120 dB (fourth series of tests), the subjects presented drastic and significant increase in vibrosensitivity, slow recovery thereof, excessive increase in maximum muscular strength and static endurance, appearance of unpleasant sensations in the region of the hands--paresthesia, pain, etc.

Thus, 120 dB should be adopted as the permissible level of local low-frequency vibration under water with total duration of dive of no more than 2 h.

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EFFECTS OF HYPOKINESIA ON INDUCTION OF BONE TUMORS

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[Abstract] Investigations were undertaken on 148 rabbits to evaluate the effects of hypokinesia on the induction of osteosarcoma by the injection of 7,12-dimethylbenzanthracene into the tibial metaphysics. For immobilization the animals were placed into 46 x 17 x 19 cm holding boxes for 23 h per day; the animals were injected with the carcinogen either concomitantly with initiation of hypokinesia (Group I), 15 (II) days or 60 (III) days after hypokinesia. A fourth group was treated only with the carcinogen. The results showed that the onset of osteosarcoma in groups I, II, III, and IV was detectable 125, 113.9, 124.5 and 197.6 days after the injection. In addition, the hypokinetic animals displayed thymic atrophy and adrenocortical hypertrophy. The overall incidence of osteosarcoma did not vary significantly among the groups. The results were interpreted to indicate that hypokinesia favored carcinogenesis, via a combination of mechanisms involving stress (elevated corticoid excretion) and immunodeficiency(thymic atrophy).
Figures 2; references: 10 Russian.
[228-12172]

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CONSTITUTIONAL ANOMALIES OF THE BRAIN AS BIOLOGICAL COMPONENT IN MECHANISM OF MENTAL ILLNESS

Kiev VRACHEBNOYE DELO in Russian No 4, Apr 82 (manuscript received 15 Sep 81)
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[Abstract] Neurologic, radiologic and EEG studies on a large cohort of patients with schizophrenia, manic-depressive syndrome, and depression have

provided evidence for the presence of "microorganic" constitutional anomalies of the brain and the cranium. Such anomalies also frequently appear in siblings and other close relatives. The available correlation of findings indicates that such anomalies may underline or predispose mental disorders, and the concept of the constitutional brain anomaly syndrome (CBAS) is therefore advanced as a nonspecific basis for the various nosologic forms of mental illness. Although CBAS is not a manifestation of disease per se, it may serve as an indication of such predisposition. References: 10 Russian.
[251-12172]

UDC 612.45 + 612.884

FUNCTIONAL STATUS OF SYMPATHETIC-ADRENAL SYSTEM IN RATS IN NOCICEPTIVE STRESS

Leningrad FIZIOLOGICHESKIY ZHURNAL SSSR IMENI I. M. SECHENOVA in Russian
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[Abstract] A comprehensive study was made of the functional status of the sympathetic-adrenal system under nociceptive stress (5 hours) in rats: dynamics of catecholamine content in the regulatory parts of the system and in peripheral organs were compared, and synthesis and neuronal capture of norepinephrine and sensitivity to norepinephrine in isolated organs (myocardium, small intestine, vas deferens, corpus striatum, hypothalamus, adrenals) were assayed at various periods (2 and 24 hours and 2, 5 and 10 days) following cessation of stress. Findings showed that catecholamine content fell 23-35% in all organs studied, except the vas deferens, immediately after stress, and for the next 2 days; norepinephrine levels were elevated in the adrenals after 24 hours; in the myocardium and small intestine norepinephrine levels reached minimums after 1 day. In subsequent periods catecholamine content increased in all organs, reaching 80-90% of initial levels after 5 days. Neuronal capture of H3-labeled norepinephrine dropped 42% immediately following stress, remaining at this level for 2 days, and then reaching 87% normal after 5 days. The postsynaptic wing was also studied with regard to epinephrine sensitivity in the vas deferens and small intestine. Findings are discussed with reference to regulatory and compensatory adrenal functions. Figure 1; references 16: 11 Russian, 5 Western.
[283-9642]

UDC 612.014.4:615.5

CHEMICAL (DRUG) STRESS--A QUALITATIVE EVALUATION OF TOXIC EFFECTS OF PHYSIOLOGICALLY ACTIVE SUBSTANCES

Moscow IZVESTIYA AKADEMII NAUK SSSR: SERIYA BIOLOGICHESKAYA in Russian
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[Abstract] Investigations were conducted on outbred male rats to establish the physiological parameters reflecting unsatisfactory adaptive responses following administration of various doses of drugs. Establishment of the threshold levels at which drugs induce homeostatic changes should provide a more sensitive indicator of drug toxicity than the currently-employed determinations of LD values. Actual evaluation of 38 drugs with respect to induced changes in the ECG, the respiratory rate, systolic blood pressure, and plethysmographic findings showed that an overall parameter can be derived which represents a summation of individual changes in the parameters in question. The numerical value so derived can be correlated with an adequate adaptation to the stressful agent (i.e., drug), strained adaptation, decompensation, and breakdown of adaptive mechanisms. References 40: 6 Western, 34 Russian.
[319-12172]

UDC: 577.391:576.314

STRUCTURAL CHANGES IN PLASMA MEMBRANE UNDER INFLUENCE OF IONIZING RADIATION

Moscow USPEKHI SOVREMENNOY BIOLOGII in Russian Vol 93, No 2, Mar-Apr 82 pp 183-195

[Article by B. S. Fomenko and I. G. Akoyev, Institute of Biological Physics, USSR Academy of Sciences, Pushchino, Moscow Oblast]

[Text] There is discussion of changes that arise in the oligosaccharide layer of the surface of the cell membrane, in the protein and lipid phases of membranes under the influence of radiation, as well as possible schemes of formation of structural changes in the membrane.

Introduction

In connection with the advances in general investigation of structure and function of biological membranes, in the last few years there has been overt progress in the field of membrane pathology. Suffice it to mention that more than half the works cited in this article, which deal with the effects of ionizing radiation on membranes, are referable to the last 4-5 years. In recent years, radiobiological research was focused on the study of molecular bases of structural membrane changes induced by radiation, as well as determination of their role in development of cell pathology. In addition, studies have begun of the influence of the state of irradiated cell membranes on their radiosensitivity.

We have made an effort here to summarize the experimental data available to us concerning structural changes in the plasma membrane of irradiated cells and describe the possible mechanisms of these changes, which ensue from these data. We hope that this will be instrumental in formulating new objectives for future research in this direction, and that it will be useful in interpreting the changes in permeability of the plasma membrane, recognition reactions, response of irradiated cells to exogenous regulatory factors and other disturbances related to the plasma membrane, which are observed in the postradiation period.

Superficial Oligosaccharides--Glycocalyx

Oligosaccharide chains of glycoproteins form a distinct near-membrane layer on the outer surface of the plasma membrane. Its thickness can reach 30 nm in an erythrocyte membrane [132]. For the sake of comparison, let us mention

that the thickness of the lipid bilayer is 6-7 nm, while that of the membrane, including protein layers, is 9 nm, as demonstrated by electron microscopy. The oligosaccharide chains have sialic and neuraminic acids and chondroitin sulfate at their ends, whereas the erythrocyte membrane contains only sialic acid. These residues given the cell surface a negative charge [126].

In most studies, the electrokinetic potential of cells served as the chief source of information about the effects of ionizing radiation on the oligosaccharide layer. The electrokinetic potential of colloid systems is highly radiosensitive: oscillating fluctuation of potential on them was observed after radiation doses of hundredths and tenths of a Gy* [53], gave grounds for Bacq and Alexander [1] for an optimistic assessment of the prospects of using this criterion in radiobiological studies. It was assumed that, if the electrokinetic potential of cells would demonstrate such high radiosensitivity, a number of changes on the membrane and cell levels could be attributed to this effect of radiation. We succeeded in finding a preliminary report [124], as well as a reference [63] to the research of Japanese radiobiologists, who demonstrated oscillating vibration of the cellular surface potential after exposure to low doses of radiation. We do not know of any subsequent publications by the above-mentioned authors in this field. In other studies, which we shall discuss below, the nature of the radiation-induced change in surface charge was basically different from the one observed in colloid systems.

It has been established that a reduction of quantity of negatively charged groups on the cell surface is demonstrable immediately after irradiation only when very high doses are used: 200-800 [125] and 2000-4000 Gy [99]. In the latter instance, we cannot rule out the contribution of radiation-induced destruction of carbohydrates to the observed effect. With lower doses, there was no change in quantity of negatively charged groups directly after irradiation on the surface of examined cells (mouse L cells, mouse fibroblasts, monkey kidney cell culture in monolayer, erythrocytes, Ehrlich's ascites tumor cells and others) [68, 106, 107, 110, 118, 125]. However, there was a decrease in electrophoretic motility during postradiation incubation of cells [68, 74, 105-107]. A maximum decline of potential occurred after incubation for 4-6 h; with higher doses of radiation, there was more intensive decline of surface potential. This process was also related to radiosensitivity of the cells. Modifiers of radiation damage affected the lethal effects of radiation and radiation-induced change in cell surface charge in the same direction [75, 100, 104]. The change in the cell surface developing in the postradiation period could be demonstrated by a method that is more sensitive than measurement of electrokinetic potential, which is based on recording the accessibility of superficial carbohydrate receptors for binding of labeled lectin [64].

An attempt was made to attribute the decrease in number of negatively charged groups on the surface of cells exposed to low doses of radiation to loss of part of their glycoproteins and carbohydrates. However, experiments revealed that the sialic and hialuronic acid, as well as chondroitin sulfate content on the surface of irradiated and incubated cells (tumor cells differing in radiosensitivity, erythrocytes and their shadows) remained at the original levels during the period of maximum decrease in electrophoretic mobility [52, 102, 103,

*1 Gy = 100 rad.

106, 107], and it is only on B and T lymphocytes that chemical techniques demonstrated migration of part of the surface glycoproteins to the supernatant [36]. Since the amount of glycoproteins and carbohydrates migrating to supernatant was obviously insufficient to explain the decrease in levels thereof on the surface, the authors [36] concluded that this process is not the prime one in postradiation damage to the surface, even in such radiosensitive cells as lymphocytes.

Most researchers view the occurring changes from the standpoint of structural reorganization of membranes [36, 63, 74, 102, 107, 109]. The following facts are in favor of such reorganization. The amount of carbohydrates responsible for the negative surface charge is not, as we have just stated, subject to appreciable changes. After irradiated cells were treated with neuraminidase, hyaluronidase and chondroitinase during the period of maximum decline of electrokinetic potential, i.e., with enzymes that split sialic and hyaluronic acids and chondroitin sulfate, the electrophoretic motility of cells decreased to the same levels as motility of nonirradiated cells treated with the appropriate enzymes [107]. Blocking the carbohydrate receptors of the cell surface with lectins prior to irradiation prevented the radiation-induced decline of electrokinetic potential [101, 102, 109]. When lectins were added at different postradiation times, the decline of electrokinetic potential stopped for a while at the level reached at the moment of lectin treatment. The profiles of pH dependence of electrophoretic mobility of irradiated and nonirradiated cells did not coincide [52]. There was a maximum postradiation decrease in quantity of negatively charged groups on the surface during incubation at 20° or higher, and none at 10-12° [101, 106, 107, 111]. The range of temperatures from 10 to 20° corresponds to the region of phase transfer of membrane lipids of most cells. The magnitude of demonstrable difference between electrokinetic potential of irradiated and nonirradiated cells is a function of ionic strength of the recording medium [99, 106, 107].

Among other effects of radiation on the carbohydrate layer of the membrane, we should mention depression of Ca^{2+} binding capacity in the postradiation period [99, 123]. On the cell surface, Ca^{2+} binds primarily with negatively charged residues of the oligosaccharide layer [128].

The data, which we discussed above, were obtained on cells exposed to radiation in vitro. Comparative experiments, which were conducted on thymocytes exposed in vitro and in vivo to radiation in sublethal dosage for animals, revealed that in both cases the magnitude of their surface charge diminished after irradiation at about the same rate and to about the same extent [7, 80]. Lectin bonding by carbohydrate receptors of blood lymphocytes exposed to radiation in a sublethal dose for animals [66] and cells irradiated in vitro [67] was impaired in a similar way. We have no data to indicate that there is a different behavior in carbohydrates of the oligosaccharide layer of the membrane surface after irradiation of cells in vitro and in vivo.

Thus, the main effects of radiation on the carbohydrate layer of the cell surface that have been described in the literature are as follows: decrease in number of negatively charged groups on the surface, inhibition of Ca^{2+} binding capacity and impaired accessibility of carbohydrate receptors for lectins. Perhaps, the same mechanisms that affect shielding of carbohydrate receptors

are also involved in impairing immune properties of irradiated lymphocytes [47, 48, 88]. Apparently, loss of glycoproteins from the surface [36], slower synthesis thereof in Golgi's apparatus [66] and impaired transport from the site of their synthesis in the cell to the cell membrane [67] could make some contribution to these radiation effects (on radiosensitive cells); however, in the opinion of these and previously cited authors, the main process is structural reorganization of the membrane, in which some of the charged carbohydrate groups on the surface shift to deeper membrane layers. According to estimates made by Japanese researchers [102, 107], based on the dependence of electrokinetic potential on ionic strength of recording medium, after irradiation of cells some of the negatively charged groups migrate from the superficial layer of 0-0.9 nm to a depth of 1-1.6 nm. (The authors used the mathematics developed for colloid systems in their calculations.)

Membrane Proteins

It is unlikely that anyone questions the fact that membrane proteins undergo structural changes in the postradiation period. This is indicated, in particular, by the results of studies of cooperative and conformational properties of membrane enzymes [14, 20, 29]. It is a more complicated matter to state how the protein changes occur, which protein groups are involved, etc.

The external surface of the lipid bilayer of the erythrocyte membrane (see Figure 1) is covered with integral protein (band 3 on electrophoregrams; it constitutes 25-27% of all membrane proteins), which bisects the bilayer, and the glycoprotein, glycophorin A, which also traverses the hydrophobic part of the membrane [71, 117]. It is assumed that the protein layer of the outer surface of the membrane is 1 nm thick [132]. Part of the molecule of the main integral protein and glycophorin A, spectrin, an actinoid protein and, perhaps, glucose-6-phosphate dehydrogenase are situated on the inner surface of the lipid bilayer. The other membrane proteins are minor ones.

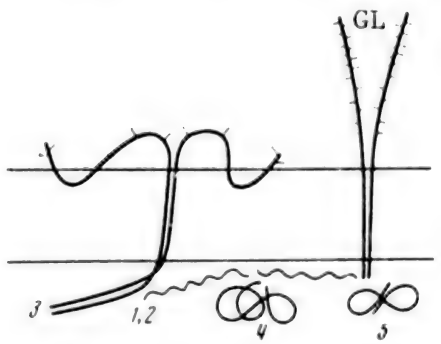

Figure 1.
Diagram of structure of erythrocyte membrane

Main membrane proteins:
1, 2) spectrin
3) main integral protein
4) actinoid protein
5) glyceraldehyde-3-phosphate dehydrogenase
(Proteins numbered 1-3 correspond to bands on electrophoregrams in a system of dodecylsulfate and polyacrylamide gel; proteins 4 and 5 are represented by bands 5 and 6; band 4 corresponds to unidentified proteins)
GL) the glycoprotein, glycophorin A
The short lines on GL and protein in band 3 refer to carbohydrate chains

It was determined that there is a decrease in number of SH groups of overall membrane proteins after in vitro irradiation of erythrocytes or membrane preparations [8, 84, 114, 119, 120]. This decrease is related to formation of disulfide bonds [8, 81], which implies involvement of SH groups in structural

changes in membrane proteins. An analogous decrease in number of SH groups was demonstrated on the outer surface of the lipid bilayer of Ehrlich's ascites cells [37] and erythrocyte membrane, where SH groups are referable mainly to the principal integral protein [114, 120]. In these experiments, registration of superficial SH groups was made using p-chloromercuribenzenesulfonate, which does not penetrate through the membrane [49]. Are disulfide bonds formed in the surface layer of proteins? We have no data on this score.

In the postradiation period, there is also a change in accessibility of protein amino groups for labeling with medium counterion, 2,4,6-trinitrobenzenesulfonic acid (TNBS). This reagent is specific for amino groups, with which it forms covalent bonds; the erythrocyte membrane is not permeable for it [55]. Consequently, the data obtained with its use are referable to amino groups of proteins of the external membrane surface. It has been established that with TNBS labeling of erythrocytes in vitro or those obtained from irradiated animals [30, 31] there was an appreciable decrease in quantity of label bound by membrane proteins. The radiation effect was demonstrable 15-30 min after exposing animals to the minimum absolutely lethal dose of radiation. The maximum difference between irradiated and nonirradiated erythrocytes was observed in the case of brief incubation of erythrocytes with TNBS. With increase in staining time, there was gradual increase to the control level of tracer incorporation in proteins of irradiated erythrocytes. This shows that increasing shielding, perhaps by the oligosaccharide layer above them, rather than deamination of proteins played the leading role in reducing the amount of protein-bound TNBS.

Our data on accessibility of protein amino groups for TNBS conform well with the results of erythrocyte studies using the method of lactoperoxidase iodination [122]. This method is specific for superficial proteins, and the enzyme does not penetrate through the lipid bilayer. On the erythrocyte surface, the tracer is bound almost exclusively with the tyrosine of the main integral protein. Experiments have shown that there was depression of protein labeling after irradiation of erythrocytes. Authors attribute this radiation effect to changes in the membrane, which make access to proteins difficult for lactoperoxidase.

It is not deemed possible to explain the diminished accessibility of tyrosine to lactoperoxidase by its migration to a more hydrophobic environment. As shown by experiments involving irradiation of erythrocyte shadows, even in doses that are sublethal to radiosensitive mammals, the parameters of fluorescence of tryptophan (intensity, long-wave shift and polarization of fluorescence) presented changes upon excitation of tyrosine and tryptophan that are inherent in a decrease in hydrophobism of the environment [135, 136]. The distance between tyrosine and tryptophan residues increased. There are no grounds to believe that this effect is related to formation of disulfide bonds, since radiosensitizing agents that react with SH groups (N-ethylmaleimide and dithiopyridine) have the same effects. Finally, although these results were obtained on irradiated membrane preparations, rather than membranes of irradiated cells, it can be assumed that with irradiation of cells the membranes will also undergo analogous changes, since fluorescence of whole cells demonstrated similar changes [77, 89].

Of the other changes induced by radiation in plasma membranes, we should mention the decrease in immobilization of spin-maleimide tracer on SH groups [54, 70], as well as greater accessibility of proteins of the external erythrocyte surface to proteolytic enzymes--trypsin, papain, chymotrypsin and pronase, but not carboxypeptidase [83]. Erythrocytes that have not been previously damaged in any way are not attacked by these enzymes. Other studies of Ehrlich's ascites tumor yielded findings, which the authors [74] interpret as an increase in accessibility of membrane lipoprotein lipase to activation by heparin. Finally, it can be concluded, on the basis of studies of immune properties of irradiated cells, that there is less lateral diffusion of membrane glycoproteins in the postradiation period [27, 47, 48].

Thus, all proteins of the plasma membrane demonstrated postradiation oxidation of sulfhydryl groups with formation of disulfide bonds, increased motility and depression of lateral diffusion of proteins, as well as change in their conformation. Moreover, it was demonstrated that proteins of the outer surface are more accessible to proteolytic enzymes and there is greater shielding of some groups (amino groups and tyrosine residues). For this reason, we cannot rule out the possibility that the decrease in number of SH groups on the outer surface is also related to greater screening thereof in the molecule or layers situated above them.

Lipid Phase

Cell and membrane lipids have been the subject of many radiobiological studies. The results thereof have been repeatedly discussed in the literature [5, 6, 17]. The main conclusion of these studies is that activation of peroxidation of lipids (POL) in the postradiation period is no exception for the plasma membrane as well [15, 54, 82, 85, 9, 95, 119]. The presence of oxygen is a mandatory condition for activation of POL. It is assumed that POL activation occurs during irradiation in the course of interaction between radiation-induced fatty acid radicals and oxygen, and that a free-radical chain mechanism is involved.

However, our experiments with erythrocyte membranes revealed that the presence of oxygen during irradiation is not a mandatory condition for postradiation activation of POL, and activation is possible even after irradiation under anoxic conditions. The Table shows that the level of products that react with thiobarbituric acid immediately after irradiation of erythrocyte membrane preparations does not differ from the base level. However, there was accumulation of POL products during postradiation incubation, in the case of exposure to radiation in both the presence and absence of oxygen. In the case of irradiation under anoxic conditions, 3-4 times larger doses than in the case of irradiation in the air were needed for the same degree of POL activation. It should be stressed that POL activity with irradiation under anoxic conditions was the same when oxygen was added to the samples right after irradiation or after incubation at 37° for 5 h. Apparently, the levels of free radicals were substantially lower in the incubated samples than right after or during irradiation. Finally, addition of EDTA or methylene blue to erythrocyte shadows right after irradiation in air or anoxia suppressed virtually entirely the postradiation activation of POL in both cases. The mechanism of the inhibiting effects of EDTA and methylene blue on POL has been well-studied, and it consists

of depression of Fe^{2+}-dependent initiation of chains of oxidation of unsaturated fatty acids. In the case with erythrocyte shadows, this may be Fe^{2+} of hemoglobin. The impression is created that, when membranes are irradiated in the presence or absence of oxygen, conditions appear in the membrane, first of all, that favor POL activation, whereas activation itself emerges as the consequence of acceleration of the process of peroxidation of lipids, which is continuous in membranes, during which initiation of chains occurs by means of the usual mechanisms.

Effects of irradiation conditions and postradiation incubation of erythrocyte membranes on level of malonic dialdehyde (MDA)

Variant	MDA, mM/100 mg protein	
	1	2
Control	18.5±1.1	21.9±1.2
0.25 kGy in air	18.8±0.8	39.1±1.2
Same + 2 mM EDTA after irradiation	-	23.4±2.1
Same + 50 μM methylene blue after irradiation in	-	25.2±4.0
dose of 1 kGy in anoxia + O_2 immediately after irradiation	18.7±0.7	42.3±2.7
1 kGy in anoxia at 37° + O_2 5 h after anoxia	18.3±1.1	42.3±2.3
1 kGy in anoxia + 2 mM EDTA after irradiation	-	24.7±1.5
1 kGy in anoxia + 50 μM methylene blue after irradiation	-	26.4±3.1

Note: 1) right after irradiation
2) after incubation for 5 h at 37° in the presence of O_2

It was also established that Ca^{2+}, Triton X-100, pronase, neuraminidase, p-chloromercuribenzenesulfonate, dithiotreitol and several other agents affect the postradiation rate of POL. All of them are membrane-active agents, which are capable of modifying its structural state. It can be assumed that one of the conditions instrumental in activation of POL is the structure-modifying effect of radiation. The question of involvement of the so-called structural factor in regulating the rate of POL has been discussed repeatedly in the literature [6, 9, 10, 17, 18, 22, 26, 57, 58, 129, 136]. As shown by radiobiological studies, the motility of the lipid phase, measured by fluorescent and spin probes, increased after exposing membrane preparations to ionizing radiation [15, 41, 46, 54, 70, 94, 95, 134], and there is also increase in rotatory [135] and lateral [136] diffusion of fatty acid chains and phospholipids. Consequently, there is an increased probability in irradiated membranes that unsaturated fatty acid bonds will be in a state that is more susceptible to oxidation. With high doses of radiation, a change in mobility of the lipid phase is demonstrable immediately after exposure, and with low doses it develops some time after exposure [134].

Perhaps, the influence of the structural factor on POL rate is mediated by a change in conformation of unsaturated bonds of fatty acid chains [92], which can be affected by the state of the lipid phase. In this and other studies [54, 70], the membranes were irradiated in the presence of oxygen. Consequently,

activation of POL could be the cause of changes in mobility of lipids. However, this interpretation for the change in lipid mobility does not apply to the instances where membrane preparations were irradiated under anoxic conditions [95].

In conclusion, we should like to note that the rate of POL and mobility of the lipid phase are interrelated processes. In the radiobiological literature, emphasis is usually laid on the role of the process and products of POL in membrane damage, and the central place in activation of POL is given to the stage of interaction between radiation-induced fatty acid radicals and oxygen. We tried to stress, in our selection of literature, that this mechanism of POL activation in the postradiation period is, at least, not the only one, while the radiosensitizing effect of oxygen, including activation of POL, is not limited to its involvement in oxidation of fatty acids under the influence of radiation. It appears quite likely that the radiation-induced structural changes in membranes also serve as a factor in activation of POL, on the one hand, and on the other hand they could be the consequence of POL activation.

Possible Schemes of Membrane Disturbances

The data available to us enable us to maintain unequivocally that the postradiation changes in membranes are not necessarily due to impairment of intracellular processes. As shown by studies of irradiated membrane preparations, they undergo the same changes (decrease in number of sulfhydryl groups, hydrophobism of tryptophan environment, Ca^{2+}-binding capacity, quantity of negatively charged groups on the surface, change in mobility of lipid and protein phases, activation of POL, etc.) as after irradiation of cells [8, 46, 54, 70, 78, 79, 106, 119, 123, 134, 135]

The hypothesis has been advanced to explain the decrease in surface charge, according to which some of the charged carbohydrate residues mechanically shift after irradiation from the external membrane surface to a depth of 1-1.6 nm [102, 107]. Protein SH groups are involved in the migration of charged surface groups to deeper levels [51, 100, 108]. Perhaps, contractile proteins play some part in this process, as they displace glycoproteins vertically, in relation to the membrane [107, 108].

However, this is far from a complete scheme, since it does not take into consideration the complex nature of correlations between membrane molecules. Thus, strong electrostatic interactions are observed between polar heads of phospholipids, phospholipids and proteins, phospholipids and sialic acid of glycoprotein, within the proteins, between sialic acid and proteins [71-73, 127]. And the vertical shift of proteins could be due to change in mobility of the lipid phase [42], whereas change in lipid-protein interactions that do not affect lipid mobility could lead to a decrease in surface charge [133]. Considering these distinctions, a static scheme of structural change in the plasma membrane in the postradiation period could include the following: a) impaired continuity of superficial layer of the membrane, perhaps due to formation of glycoprotein clusters; b) intensification of noncovalent interactions between sialic acid residues, on the one hand, and proteins and phospholipids, on the other; c) attenuation of lipid-protein interactions; d) increased mobility of acyl chains in the hydrophobic region. From the standpoint

of this scheme, it is not difficult to explain many experimental facts, including appearance in the irradiated membrane of sensitivity to proteolytic enzymes, intensification of screening of the protein groups studied (amino groups and tyrosine residues) against labeling, attenuation of phospholipid shielding, decrease in surface charge, as well as the radiation-induced increase in sensitivity of plasma membranes to detergents [87, 112], diminished osmotic stability of erythrocytes [21, 34], acid [2, 3] and alkali resistance [28], resistance to hydrogen peroxide [59], which we did not discuss above.

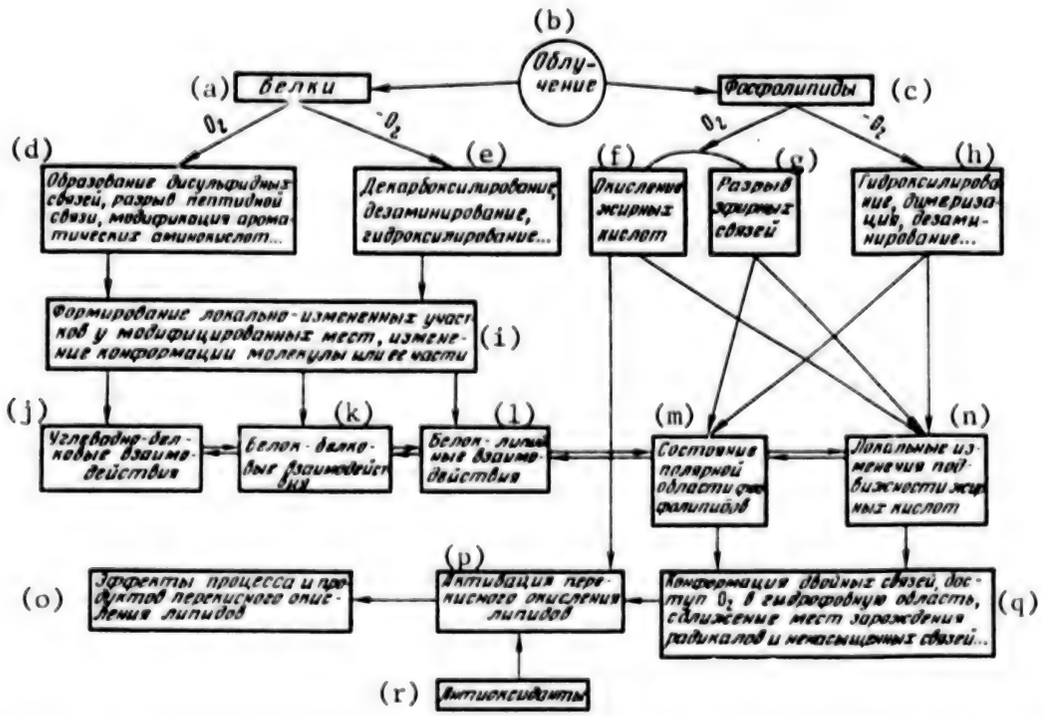

Figure 2. Possible sequence of radiation-induced events in plasma membrane

Key:

a) proteins
b) irradiation
c) phospholipids
d) formation of disulfide bonds, break in peptide bond, modification of aromatic amino acids....
e) decarboxylation, deamination, hydroxylation
f) oxidation of fatty acids
g) break in ester bonds
h) hydroxylation, dimerization, deamination....
i) formation of locally altered regions in modified areas, change in conformation of molecule or parts thereof
j) carbohydrate-protein interactions
k) protein-protein interactions
l) protein-lipid interactions
m) state of polar region of phospholipids
n) local changes in fatty acid mobility
o) effects of process and products of peroxidation of lipids
p) activation of lipid peroxidation
q) conformation of double bonds, O_2 access to hydrophobic region, approximation of sites of generation of radicals and unsaturated bonds....
r) antioxidants

In making the dynamic diagram (Figure 2), we took into consideration the fact that the POL activation factor could consist of structural disturbances in the membrane occurring under the effect of radiation, as well as the high radiosensitivity of the protein phase of membranes. At the present time, vast material has been accumulated concerning the relative radiosensitivity of the protein and lipid phases of membranes. On this basis, several authors consider the protein phase to be more radiosensitive than the lipid one. To back up their view they cite the following facts. It has been established that disturbances are demonstrable in the protein phase with lower radiation doses than those required for the lipid phase [41, 46, 115, 120, 121, 134-136], according to the criteria of change in level of SH group and POL rate, as well as physical parameters of membranes recorded by means of spin and fluorescent probes (mobility, microenvironment). The authors of these studies believe that SH groups are the chief target of the membrane. Many facts confirming the important role of protein SH groups in radiation damage to membranes were obtained with the use of SH reagents [39, 43, 45, 81, 114, 115, 120]. It was demonstrated with erythrocytes, thymocytes and other cells that SH blocking agents, both those that penetrate through the membrane (N-ethylmaleimide, p-chloromercuribenzoate and others) and that do not penetrate it and, consequently, which react with SH groups of proteins of the external membrane surface (p-chloromercuribenzenesulfonate and bis-(2-guanidoethyl)-disulfide), increase radiosensitivity of membranes according to several parameters, including POL activation [85, 119]. These agents per se, without irradiation, have an effect on membranes that is similar to that of radiation, and they are capable of modifying damage when used in the postradiation period. Several authors observed additivity of effects of radiation and SH blocking agents [81, 91]. Since various molecules participate in reactions with protein SH groups under the influence of SH blocking agents and radiation, it can be assumed that, in both instances, there is impairment of protein organization and, if we consider POL activation, lipoprotein structures as well, wherein the similarity of effects of these two factors is expressed.

We can single out the following stages of formation of changes in the membrane: 1) Appearance during irradiation of modified groups in membrane molecules, that are related to hydroxylation, decarboxylation and deamination in the case of exposure without oxygen, and oxidation of fatty acids, break of ester bonds in phospholipids in the case of irradiation in the presence of oxygen [19, 25, 61, 81, 113]. 2) Stage of generation. It includes appearance of local altered regions in the molecule at the impaired sites, involvement in this process of spatially adjacent regions of this and adjacent molecules, impaired interaction with lipids, local change in state of phospholipids. Analogously, in the lipid phase, formation of a locally altered region is possible at the sites of injured polar or nonpolar parts of the phospholipid. It should also be borne in mind that, by virtue of the complex interactions between molecules in the membrane, there may be a reverse process--intensification of changes in radiation-modified sites [29]. 3) Activation of POL. The cause may be free radicals induced by radiation. Nor can we rule out the usual mechanisms of initiation of POL, which are affected by the structural state of membranes [6, 9, 10, 17, 18, 22, 26, 57, 58]. The role of POL in membrane damage is well-known. Finally, in view of the fact that the reciprocal location of molecules in the membrane depends on the magnitude of

transmembrane potential [90], one must consider the possibility of involvement of radiation-induced decline of membrane potential in postradiation change in the membrane [32, 33, 38, 50].

In constructing the diagram of processes in irradiated membranes, consideration was not given to the fact that intracellular processes in cells may affect the membranes, enhancing the radiation effect or causing restoration of membranes. Thus, when irradiated erythrocytes (but not erythrocyte membrane preparations), Ehrlich's ascites cells, lymphocytes and other cells are incubated, the reduction of surface charge and in number of glucose-mannose receptors in the first 4-6 h of incubation is followed by restoration of charge and number of receptors after 24 h [64, 74, 100, 105, 106, 110].

In such specialized cells as erythrocytes irradiated in vitro, there was restoration of SH group level, even after exposure to radiation in doses of hundreds of grays [8, 81, 119], membrane permeability [81] and, according to our data, accessibility of amino groups of proteins of the external surface to trinitrobenzenesulfonic acid. Presence of an energy substrate in the incubation medium and incubation at temperatures, at which there are active intracellular processes are mandatory conditions for recovery processes. Restoration of the erythrocyte membrane is associated with activation of synthesis and incorporation in the membrane of phosphatidic acid, the only phospholipid capable of synthesizing erythrocytes [56].

Conclusion

Alper [35] advanced the conception of a membrane as one of the targets in radiation-induced inactivation of the cell. The results of studies of the effects of ionizing radiation on the structure of the plasma membrane are in complete agreement with this view. It was found that the plasma membrane is a highly radiosensitive component of the cell, which responds analogously to radiation when cells and membrane preparations are exposed, according to several parameters. In both instances, radiation doses comparable to sublethal doses for mammals are sufficient for induction of changes. Experiments on lymphoid cells revealed the same changes in membranes after in vitro and in vivo irradiation [74, 75, 77, 80]. In this regard, it is tempting to assume that the radiation-induced changes in the plasma membrane may make some contribution to inactivation of cells when they are irradiated in vivo as well. However, additional experiments are required to make this conclusion.

The research that we have discussed here shows that postradiation changes in the cell membrane are referable to numerous bonds. Without analyzing the experimental data obtained from experiments with factors other than radiation, let us mention that many of these changes can be readily simulated in cells and membrane preparations, and they are explainable from the standpoint of structural reorganization of the membrane, which is associated with change in conformation of membrane molecules and intermembrane interactions. We believe that primary radiation damage to membrane molecules, which is related to oxidation of fatty acids and SH groups, break of ester, peptide and hydrogen bonds, modification of different groups, etc., may play the part of inductor of structural changes. Judging from the glycocalyx, the changes induced by low doses of

radiation are reversible. This is not associated with POL activation. It is observed after exposure to high doses of radiation and, in our opinion, considering the numerous data on the effect of the structural factor on POL [6, 9, 10, 17, 18, 22, 26, 57, 58], we cannot rule out involvement of radiation-induced structural changes in the membrane in activation of POL via mechanisms that are common to other forms of pathology.

Is there a link between radiation-induced changes in the plasma membrane and disturbances of cellular processes, and what is the nature of this link? We can answer these questions unequivocally only with regard to ion homeostasis of cells. Most researchers agree that the intensification of flow of K^+ from cells and Na^+ into cells, which is observed in the postradiation period, is attributable mainly to structural changes in the membrane, as a result of which the membranes are more permeable to ions. The experimental research on this question has been discussed comprehensively before [91].

The postradiation changes described for the cell membrane are not specific to this type of membrane, and they are observed on the membranes of intracellular organelles. Thus, the negative charge of nuclei of irradiated lymphoid cells diminishes, just like the decrease in charge of the cells themselves [103]. There are data to the effect that there is a decrease in number of SH groups in various cell organelles after irradiation of animals, cells or cell organelle preparations [11, 23, 130], changes in mobility of lipid and protein phases [5], attenuation of lipid-protein interactions [4] and shielding of cell organelle phospholipids, which is demonstrable by the accessibility of phosphatidylethanolamine to labeling with trinitrobenzenesulfonic acid [13], increased sensitivity of membrane preparations to POL induction with Fe^{2+} [24]. Consequently, the patterns described for the plasma membrane are applicable to development of postradiation changes in membranes of intracellular organelles as well.

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EFFECTS OF COMBINATION OF ANTIBIOTIC-RESISTANT BIFIDOBACTERIA AND CORRESPONDING ANTIBIOTICS ON SURVIVAL OF IRRADIATED MICE

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[Article by V. M. Korshunov, B. V. Pinegin, N. P. Ivanova and V. N. Mal'tsev, First Moscow Medical Institute imeni Pirogov and Institute of Biophysics, USSR Ministry of Health]

[Text] Broad-spectrum antibiotics are used to treat intestinal dysbacteriosis of diverse etiology, including postradiation dysbacteriosis [1]. Antibiotic therapy is instrumental in decontaminating the intestine. In addition to pathogenic microorganisms, there is disappearance of lactobacilli and bifidobacteria [8, 10] which, as we know, perform several important and useful functions [2-4, 7, 9, 12, 13]. For this reason, in addition to antibiotics, bifidobacterial preparations are used to restore the microbial cenosis [4, 6], and administration thereof is started after antibiotics are discontinued. There are some flaws to deferred administration of bifidobacteria, since the process of colonization of the intestine with commercial bifidobacterial preparations is rather lengthy, and there is slow elevation of bifidobacterium level in the intestinal tract, whereas exogenous recontamination of the intestine by conditionally pathogenic bacteria is possible after antibiotic therapy is discontinued. On the other hand, use of antibiotics alone could, in turn, be the cause of intestinal dysbacteriosis.

Our objective was to eliminate intestinal dysbacteriosis in irradiated animals by means of combining antibiotics and preparations of bifidobacteria resistant to these antibiotics, and thus prolong the life of these animals.

Materials and Methods

Mongrel mice, weighing 18.0-18.5 g, were exposed to radiation from a GUBE-1200 unit in a dosage of 700 R (dose rate 180 R/min). After irradiation, the animals were divided into 4 equal groups of 15-20 mice. The first group of mice was given one of the tested antibiotics (kanamycin, gentamycin, ampicillin) intragastrically and bifidobacteria resistant to the antibiotic used; the second group was given only antibiotics at the same times; the third group received only bifidobacteria and the fourth group was given sterile saline. The programs of administration of antibiotics and bifidobacteria were the same for the

first three groups of mice. The daily dose of kanamycin was 1 mg, ampicillin 1 mg and gentamycin 20 μg. The daily dosage of antibiotic-resistant bifidobacteria was 1×10^9 cells. We used bifidobacterial strain D kan 100, which is resistant to kanamycin in a concentration of 100 mg/mℓ, with kanamycin. With gentamycin and ampicillin, we used strain D4a200, which is resistant to kanamycin in a concentration of 50 mg/mℓ, ampicillin in a concentration of 200 μg/mℓ, gentamycin in a concentration of 2000 μg/mℓ and monomycin in a concentration of 1000 μg/mℓ. The antibiotics and bifidobacteria were given together in a volume of 0.25 mℓ.

We tested three different programs of administration of antibiotics and antibiotic-resistant bifidobacteria. The first involved early use of antibiotics: kanamycin or ampicillin daily, from the 1st to 7th days, and bifidobacteria on the 1st, 3d, 5th, 7th, 10th, 15th and 20th days after irradiation. On the second program, the antibiotic (kanamycin) and bifidobacteria were given daily from the 5th to 20th postradiation days. On the third program, antibiotics (kanamycin, ampicillin or gentamycin) and bifidobacteria were given from the 1st to 21st postradiation days at 48-h intervals.

We tested the efficacy of each therapeutic program in 3-5 independent experiments. In all, we used 1486 mice.

Results and Discussion

Early administration of kanamycin combined with kanamycin-resistant strains of bifidobacteria on the first program prolonged survival of irradiated mice (see Table). This was demonstrable from the 16th postradiation day on, and thereafter the difference in percentage of surviving mice among treated and untreated mice increased constantly; survival rate was similar in the first 3 groups up to the 23d day, constituting 30.0±1.1% in the first group, 32.8±2.2% in the second and 32.8±1.2% in the third group on the 23d day; survival of mice in the fourth group constituted 12.8±0.9%. Subsequently, there were no deaths among mice in the first and third groups, and on the 30th day the percentage of surviving mice in these groups constituted 30.0±1.1 and 32.8±1.2, respectively. At the same time, there was some decline in survival rate by the 30th day in the second and fourth groups, when it constituted 21.4±0.9 and 8.6±0.8%, respectively.

Early administration of ampicillin combined with ampicillin-resistant bifidobacteria (first program) also elicited some therapeutic response, increasing the survival rate among irradiated animals (see Table). The therapeutic effect of ampicillin and ampicillin-resistant bifidobacteria was manifested on the 10th postradiation day, i.e., somewhat sooner than with the use of kanamycin and bifidobacteria. At this time, the percentage of surviving animals constituted 81.2±2.2, 71.9±1.5, 79.7±2.8 and 57.8±3.8% in the first, second, third and fourth groups, respectively. At subsequent observation times, there was an increase in the difference in survival rate among treated and untreated mice. The survival rate on the 18th postradiation day constituted 46.9±1.7, 34.3±1.5, 57.8±2.4 and 15.6±1.6 in the first, second, third and fourth groups, respectively.

On the 23d day, survival constituted 35.9±1.9, 26.6±1.5, 35.9±1.6 and 12.5±0.9% in the first, second, third and fourth groups, respectively; on the 30th day the figures were 28.1±1.6, 25.0±1.1, 29.7±2.2 and 7.8±0.9%.

Survival of mice exposed to ^{60}Co gamma rays in a dosage of 700 R and treated with antibiotics combined with bifidobacteria resistant to these antibiotics

Therapy	Therapy program	Total irradiated mice	Surviving mice	Survival %, M±m	Therapy program	Total irradiated mice	Surviving mice	Survival %, M±m
Kanamycin + bifidobacteria	1	70	21	30,0±1,1	3	45	15	33,3±2,9
Kanamycin	1	70	15	21,4±0,9	3	45	9	20,0±2,3
Bifidobacteria	1	70	23	32,8±1,2	3	45	12	26,6±1,7
Control		70	6	8,6±0,8		45	1	2,2
Ampicillin + bifidobacteria	1	64	18	28,1±1,6	3	65	21	32,3±0,9
Ampicillin	1	64	16	25,0±1,1	3	65	13	20,0±1,1
Bifidobacteria	1	64	19	29,7±2,2	3	65	15	23,1±0,7
Control		64	5	7,8±0,9		65	3	4,6±0,3

Deferred use of kanamycin and bifidobacteria (second program) elicited a weaker therapeutic response than the first program. Thus, on the 9th post-radiation day survival constituted 80.0±2.2, 77.7±1.6 and 53.3±2.1% in the 1st, 2d and 3d groups, respectively (Figure 1 [not reproduced]); on the 23d day the figures were 26.6±0.8, 21.1±0.6 and 12.2±1.2%, and on the 30th day 20.0±0.6, 15.5±0.4 and 11.1±0.5%, respectively.

In the next experiments we administered the agents on the third program. With use of kanamycin and strain D kan 100 bifidobacteria, mouse survival constituted 40.0±2.8, 37.7±1.8, 44.4±2.7 and 8.8±0.3% in the 1st, 2d, 3d and 4th groups, respectively, on the 16th postradiation day and 33.3±2.9, 20.0±2.3, 26.6±1.7 and 2.2% on the 30th day (see Table).

Administration of kanamycin combined with antibiotic-resistant bifidobacteria increased survival by 3.5 times, as compared to untreated irradiated animals, with use of the first program, by 1.8 times with the second and by 10 times with the third program.

With the use of ampicillin combined with an ampicillin-resistant strain of bifidobacteria on the third program the survival rate on the 18th postradiation day constituted 46.2±2.2, 32.3±1.7, 33.5±1.9 and 13.8±0.6% in the 1st, 2d, 3d and 4th groups. A statistically reliable higher survival rate among treated mice than untreated ones was demonstrable throughout the subsequent observation period. On the 30th day, the survival rates constituted 32.3±0.9, 20.0±1.1, 23.1±0.7 and 4.6±0.3 in the 1st, 2d, 3d and 4th groups, respectively (see Table). With use of the first therapy program, survival of mice on the 30th postradiation day was 3.6 times higher for animals given ampicillin and bifidobacteria,

than for untreated animals, and with the use of the third program it was 7 times higher (see Table).

Use of gentamycin and gentamycin-resistant bifidobacterial strain on the third program was also rather effective in treating postradiation intestinal dysbacteriosis.

On the 23d day, the survival rates constituted 48.0±1.9, 25.3±1.1, 42.6±2.1 and 16.0±0.7% in the 1st, 2d, 3d and 4th groups, respectively; on the 30th day, the figures were 41.3±2.2, 14.6±0.6, 40.0±1.7 and 4.0±0.4%.

Thus, the combined use of antibiotics and antibiotic-resistant bifidobacteria on the programs we tested increased the survival rate among irradiated animals. However, the intensity of the therapeutic response was largely related to the program used and the stage of development of postradiation intestinal dysbacteriosis, at which therapy began.

In our preceding studies, we demonstrated that marked intestinal postradiation dysbacteriosis develops by the 3d postradiation day and persists to the 22d-23d day [1, 5].

The least therapeutic response was observed when the agents were given starting on the 5th postradiation day, against the background of developed intestinal dysbacteriosis (second program). The response was enhanced when they were started on the 1st postradiation day and given for the next 7 days, thus preventing postradiation intestinal dysbacteriosis at the early stages of its development (first program).

The best therapeutic response, which was characterized by increase in survival rate among irradiated animals, was observed with use of the third program, when antibiotics and bifidobacteria were given from the 1st to 21st postradiation days and throughout the period of development of postradiation dysbacteriosis. Yet, administration of antibiotics alone on the same program elicited less response than in combination with bifidobacteria. Antibiotic-resistant bifidobacteria given to irradiated animals without antibiotics also had a significant effect on prolonging survival of these animals. The combined use of antibiotics and bifidobacteria for radiation sickness is validated by the fact that, in the presence of this disease when there is drastic impairment of homeostasis, there is substantial impairment of permeability of the intestinal walls, and conditionally pathogenic microorganisms, which are normally localized only in the intestinal lumen, readily penetrate into its wall, and from there the toxic products of their metabolism enter the blood stream freely. The fact that, after irradiation, there is a drastic decrease in lactobacilli and bifidobacteria lining the epithelial layer of the intestinal wall and normally preventing penetration into the wall of conditionally pathogenic microorganisms is also instrumental in penetration thereof in the intestinal wall [1, 4, 7, 11]. For this reason, antibiotics given intragastrically to irradiated animals for 21 days after irradiation help decontaminate the intestinal tract, while antibiotic-resistant bifidobacteria, which colonize the intestine, are involved in normalizing the microbial cenosis. The advantage of antibiotic-resistant bifidobacteria is that, by using them, one can effectively contaminate it with bifidoflora concurrently with sterilization of the intestine, already at the early stage of therapy.

Conclusions

1. The combined use of antibiotic-resistant bifidobacteria and corresponding antibiotics (kanamycin, gentamycin or ampicillin) results in greater survival of irradiated mice than with the use of an antibiotic alone.

2. Antibiotic-resistant bifidobacteria increase survival of irradiated mice when given without antibiotic.

3. The program of prolonged therapy, in which the antibiotic and corresponding antibiotic-resistant bifidobacteria are given to irradiated mice from the 1st to 21st postradiation days at 48-h intervals, is more effective than the program of early therapy, when the antibiotic is given from the 1st to 7th postradiation days and bifidobacteria on the 1st, 3d, 5th, 7th, 10th, 15th, 20th and 25th postradiation days and the deferred therapy program, in which the antibiotic and bifidobacteria are given from the 5th to 20th postradiation days.

4. It is more promising to use antibiotic-resistant bifidobacterial strains for treatment of postradiation intestinal dysbacteriosys than commercial bifidobacterial products, since the former can be given effectively at the same time as antibiotics.

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CSO: 1840/232

UDC: 577.391:661.879:612.015.33:612.112.94

NUCLEIC ACID METABOLISM IN RAT THYMUS UPON EXPOSURE TO γ RADIATION AND PLUTONIUM-239

Moscow RADIOBIOLOGIYA in Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 19 Dec 80) pp 35-39

YELKINA, N. I.

[Abstract] A study is made of DNA and RNA metabolism in the rat thymus over a period of 1 year after external γ irradiation and administration of plutonium-239. Experiments were performed on 134 male Wistar rats 160-170 g in four groups: 1, external γ irradiation plus plutonium; 2, plutonium-239; 3. external γ irradiation; 4, intact control. The results indicate greater changes in the thymus upon combined exposure to γ irradiation and plutonium. Highly complex interactions occur in the metabolic processes and the experimental facts observed cannot as yet be completely explained. The nucleic acid metabolic disorders detected, caused rapidly by external γ radiation, were later intensified by administration of plutonium, partially due both to the α radiation of the plutonium which is pooled in the thymus and to the indirect influence through other systems such as the bone marrow, liver and spleen which accumulate plutonium in much larger quantities. Figures 3; references 14: 13 Russian, 1 Western.
[210-6508]

UDC: 577.391:576.3

EFFECT OF LASER RADIATION ON CHINESE HAMPSTER CELLS CULTURED IN VITRO

Moscow RADIOBIOLOGIYA in Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 10 Dec 80) pp 40-43

ABDVAKHITOVA, A. K., GRIGOR'YEVA, L. N. and PARKHOMENKO, I. M.,
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[Abstract] A study is made of the influence of laser radiation on the reproductive capacity of cells, evaluated based on the formation of macroscopic colonies. Experiments are performed on Chinese hampster cells Bildii FAF-28 clone 237. Radiation was produced by a helium-neon laser (λ=633 nm) and a neodymium laser (λ=534 nm) using doses of 40 to 900-960 mJ/cm^2. The laser radiation was found to have a stimulating effect on cell survival, equal to that of noncoherent monochromatic light. Laser radiation is also capable of reducing the harmful effect of X-radiation when the laser radiation is applied in small doses. Figure 1; references 13: 6 Russian, 7 Western.
[210-6508]

UDC: 577.391:612.419

RAT BONE MARROW CFUc CONTENT DYNAMICS DURING LONG TERM FRACTIONATED IRRADIATION

Moscow RADIOBIOLOGIYA in Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 11 Aug 80) pp 44-47

LUZANOV, V. M. and MUKSINOVA, K. N.

[Abstract] A study is made of the content of rat bone marrow granulocyte precursor cells in the process of long term fractionated irradiation. Wistar rats 8 to 10 weeks in age at the beginning of the experiment, body mass 140-150 g were used, irradiated 6 days per week in an experimental γ irradiator with Cs-137 at a dose of 0.485 Gr. It was found that daily irradiation at 0.48 Gr for 60 days caused a sharp decrease in the quantity of CFUc, the degree of decrease depending on the total dose of radiation received. The change in content of these cells determines the nature of granulocytopoesis disorders in experimental rats. The decrease in nucleus-containing bone marrow cells was less than the change in CFUc content. Figure 1; references 15: 7 Russian, 8 Western.
[210-6508]

UDC: 577.391:539.125.5:591.434

COMPARATIVE RADIATION DAMAGE TO SMALL INTESTINE OF MICE EXPOSED TO X-RAYS AND FISSION NEUTRONS DURING VARIOUS STAGES OF POSTNATAL DEVELOPMENT

Moscow RADIOBIOLOGIYA in Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 2 May 80) pp 76-81

BOGATYREV, A. V., TIMOSHENKO, S. I. and SVERDLOV, A. G., Leningrad Institute of Nuclear Physics imeni B. P. Konstantinov, USSR Academy of Sciences, Gatchina

[Abstract] The work was performed on 300 CHR mice, newborn, 2 weeks, 4 weeks and 10-12 weeks of age. The animals were bombarded with fission neutrons in a mixed γ-neutron field of a VVR-M reactor, mean neutron energy 0.85 MeV, dose rate 0.25-0.3 Gr/min, neutrons representing 80% of the total dose. X-radiation was administered at 250 kV, 215 mA, 0.5 mm Cu+1 mm Al filters, skin-focal length 40 cm, dose 1.8 Gr/min. Doses were 9.8 Gr for newborns, 2 week old and 10-12 week old animals, 6.8 and 2.0 Gr for 4 week old animals. The animals were sacrificed 4 hours to 12 days after irradiation and a segment of the small intestine fixed in 10% neutral formalin. Age differences were found in the radiation damage to the small intestine. In newborns and 2 week old mice, all signs of radiation damage were less strongly expressed than in 4 week old and mature mice. Four week old mice were most sensitive to radiation, intestinal damage being the dominant factor in the mechanism of post-radiation death following neutron bombardment. Apparently the decisive factor causing the age specifics of radiation damage is the difference in the rate of renewal of cells on the villi. Figures 3; references 6: 5 Russian, 1 Western.
[210-6508]

UDC: 577.391:612.418

EA-TEST FOR EVALUATION OF FUNCTIONAL CHANGES IN SPLENOCYTES IN IRRADIATED ORGANISM

Moscow RADIOBIOLOGIYA in Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 16 Nov 80) pp 82-87

KLEMPARSKAYA, N. N. and ULANOVA, A. M.

[Abstract] A new experimental model has been developed allowing determination of early changes in the cell functioning of parenchymatous organs after administration of antigens. This model is used to show that irradiation, even in doses not causing clinical radiation disease, changes these early normal

reactions of the cells to both foreign and endogenous antigens. The essence of the model is that the cells of the organs are placed in a solution containing the antigen. Thirty to 60 minutes after immunization, the spleen and liver cells manifest in increased capacity to liberate autoantigens into the surrounding suspension fluid. The test is therefore called the autoantigen excretion or EA test. Figures 3; references 15: 12 Russian, 3 Western.
[210-6508]

UDC: 621.039.58

STUDY OF SEROTONIN LIBERATION IN VIVO BY MAST CELLS EXPOSED TO MEA

Moscow RADIOBIOLOGIYA in Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 16 Sep 80) pp 94-96

GONCHARENKO, Ye. N., GRAYEVSKAYA, Ye. E., SOBOLEV, A. S. and PYL'NIK, Ye. E.,
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[Abstract] It was earlier proposed that one source of the increased level of biogenous amines in radiosensitive tissues is amines deposited in mast cells of the connective tissue. Determination of the capability of radioprotectors to liberate endogenous amines from mast cells in the peritoneal fluid has brought out the need for determination of their subsequent fate and possible participation in the accumulation of endogenous radioprotectors in radiosensitive tissues not capable of their synthesis. This is the subject of the present study, performed on Wistar rats which were sacrificed, the fluid extracted from the peritoneal cavity in a salt solution. The cells were incubated for 120 minutes at 37°C with labeled serotonin. Incubation with ^{3}H serotonin led to significant accumulation of the amine. The results indicate that the radioprotector MEA (mercaptoethylamine HCl) causes excretion of serotonin by mast cells into the blood, increasing its content in radiosensitive tissue such as the spleen, not capable of synthesizing it. Figure 1; references 4: 2 Russian, 2 Western.
[210-6508]

UDC: 577.391:612.015.33

cAMP-DEPENDENT PHOSPHORYLATION OF PROTEINS IN TISSUES OF IRRADIATED MICE

Moscow RADIOBIOLOGIYA in Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 28 Oct 80) pp 96-99

CHIRKOV, Yu. Yu., SERBIN, P. and SOBOLEV, A. S., Biology Faculty, Moscow State University imeni M. V. Lomonosov

[Abstract] The study of the cAMP-dependent phosphorylation of proteins in the irradiated organism can answer the question as to whether disorders arising in the enzymes responsible for synthesis and hydrolysis of cAMP can cause distortions in the occurrence of cAMP-controlled metabolic processes in the cells. Male SHK mice 18-20 g were irradiated at 8 Gr in an X-ray machine with copper and aluminum filters at 0.5 Gr/min. Radiation changed the response of the cAMP system of the liver to a hormonal signal, manifested as a distortion in the process of phosphorylation of the protein substrate by cAMP-stimulated proteinkinesis. A change in intracellular cAMP concentration caused by radiation damage is not compensated and hinders cAMP-dependent phosphorylation, disrupting normal occurrence of cAMP controlled metabolic processes in the cell such as biosynthesis of proteins. References 10: 5 Russian, 5 Western.
[210-6508]

UDC 577.391

GENERAL ADAPTABILITY OF PROGENY OF IRRADIATED MICE, REPORT 2: INTENSITY OF BASAL METABOLISM IN MICE

Moscow RADIOBIOLOGIYA In Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 14 Apr 80) pp 99-102

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[Abstract] It was earlier suggested that differences in the radiation sensitivity of progeny of mice irradiated for different periods of time may result from reduced rates of metabolic processes, having a positive role in cases of acute radiation, a negative role in cases of fractionated radiation. This work checks this assumption by studying the rate of basal metabolism in mice of both groups. Body temperature, respiration and pulse frequency were tested. Reliable differences between progeny of irradiated and nonirradiated mice were found only in body temperature. Differences of the other criteria, though in the same direction, were statistically unreliable. The combination of physiological data indicates that basal metabolism rates are somewhat slowed in the progeny of irradiated mice. Figure 1; references 9: 7 Russian, 2 Western.
[210-6508]

UDC: 577.391:612.112.94:612.014.2

IRRADIATION OF HUMAN PERIPHERAL BLOOD LYMPHOCYTES IN VITRO BY ^{60}Co γ-QUANTA IN G_0 PHASE DOES NOT INCREASE FREQUENCY OF SISTER CHROMATID EXCHANGES

Moscow RADIOBIOLOGIYA in Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 25 Aug 80) pp 102-105

PYATKIN, Ye. K. and NUGIS, V. Yu.

[Abstract] A study was made of the frequency of sister chromatic exchanges in human lymphocytes irradiated in vitro by ^{60}Co γ quanta in the G_0 phase using peripheral blood samples from the same healthy donors as the control. The produced lymphocyte differed significantly in proliferative activity. No difference in the number of sister chromatid exchanges between control and experimental cultures was observed at any radiation dose. This indicates the sister chromatid exchanges, in contrast to chromosomal aberrations, cannot be used to indicate dose in acute radiation sickness. References 14: 2 Russian, 12 Western.
[210-6508]

UDC: 577.391

POSSIBILITY OF USING CERTAIN RAT ORAL CAVITY EPITHELIAL TISSUE INDICES FOR EARLY DIAGNOSIS OF RADIATION TRAUMA

Moscow RADIOBIOLOGIYA in Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 1 Nov 80) pp 106-109

SHATININA, N. N. and UNDALOVA, L. G., Central Scientific Research Roentgen-Radiological Institute, USSR Ministry of Health, Leningrad

[Abstract] The multilayered flat epithelium of the tongue and cheek has high mitotic activity, is easily accessible and highly radiosensitive. A study is made of the mitotic activity and DNA concentration in the epithelial tissue of the oral cavity in male white rats at various periods following irradiation was 3.0 Gr, 6.0 Gr and 8.0 Gr of x-radiation. With increasing time following the moment of irradiation the nature of the dose curve changes. Within 48 hours after irradiation there are no significant differences between doses of 3, 6 and 8 Gr for the lingual or buccal epithelium, though the mitotic activity does not return to the control levels. These times are therefore in the time interval during which restoration of the mitotic activity of the lingual and buccal epithelium occurs. Differences in mitotic activity are observed at 12 and 24 hours following irradiation for all three doses in comparison to the controls. Figure 1; references 11: 9 Russian, 2 Western.
[210-6508]

UDC: 577.391:612.419:612.418

DISTRIBUTION OF VARIOUS TYPES OF HEMATOPOIETIC COLONIES IN BONE MARROW AND SPLEEN OF IRRADIATED RATS AND MICE

Moscow RADIOBIOLOGIYA in Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 28 Apr 80) pp 109-112

SHVETS, V. N.

[Abstract] A comparative study is presented of the distribution of colonies in the spleen and bone marrow of rats and mice which had received bone marrow cells intravenously 3 to 5 hours after irradiation in various combinations: rat-rat, rat-mouse and mouse-mouse. Nine to 10 days after administration of the cells, the spleen and femur of the recipient were fixed in paraffin, and 5 to 7 μm sections were obtained each 50 μm, stained with hematoxylin-eosin and examined with a microscope to count erythroid, myeloid, magacariocyte, undifferentiated and mixed colonies. In mouse bone marrow, myeloid colonies were predominant, while in rats erythroid colonies were predominant. In both rat-mouse and mouse-mouse experiments, erythroid colonies predominated in the spleen, myeloid colonies in the bone marrow. References 11: 1 Russian, 10 Western.
[210-6508]

UDC: 577.391

BONE MARROW PLASMA CELLS IN DOGS WITH ACUTE RADIATION SICKNESS

Moscow RADIOBIOLOGIYA in Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 23 Apr 80) pp 112-115

VLASOV, P. A.

[Abstract] Fifty-seven of 62 dogs were exposed to ^{60}Co γ irradiation at the minimal absolutely lethal dose, then electrocuted at various times after exposure, 5 dogs each at 30 minutes, 3, 6, 18 hours, 1, 3, 7, 10, 11 and 12 days. As radiation aplasia develops in the bone marrow there is a clear increase in the absolute number of plasma cells, most of which function actively and produce immunoglobulins. The source of the plasma cells is the lymphoid organs. This phenomenon is considered a manifestation of an autoimmune state. Figures 2; references 12: 6 Russian, 6 Western.
[210-6508]

UDC: 577.391

INCREASE IN EFFECTIVENESS OF BODY WEIGHT ACCOUNTING IN RADIOBIOLOGICAL ANIMAL STUDIES

Moscow RADIOBIOLOGIYA in Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 23 Jul 80) pp 115-117

TYURIN, Ye. A.

[Abstract] A more informative method of revealing changes in body mass of animals in experimental and control groups in radiobiological experiments than simple recording of body weight is suggested: counting the number of cases of reduced body mass (in %) in comparison to the minimum initial mass of individuals used in the experiment. This requires determination of the limits of fluctuation of body mass of the animals used in the experiment, with the minimum figure used as the threshold. The data produced demonstrate the possibility of using the method suggested to evaluate changes in body mass of animals in experimental and control groups in studies of radioprotective substances on small laboratory animals. Figures 2; references: 4 Russian.
[210-6508]

UDC: 577.391:576.809.7

STIMULATION OF ANTIBODY FORMATION IN IRRADIATED ANIMALS BY ENDOGENOUS AND EXOGENOUS INTERFERON

Moscow RADIOBIOLOGIYA in Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 8 Sep 80) pp 123-126

ZHELEZNIKOVA, G. F., Central Scientific Research Roentgeno-Radiological Institute USSR Ministry of Health, Leningrad

[Abstract] Interferon and its inductors were used to restore the immune response of irradiated mice to administration of antigens. The experiments were performed on mice of both sexes subjected to full body irradiation by X-rays, dose power 9.4-11.0 Gr/min, dose 4 and 5 Gr. One day after irradiation the mice were immunized by intraperitoneal administration of sheep erythrocytes or E. coli. The immune response was tested after 4,6,10 and 15 days. Both interferon preparations, virus-induced and endotoxin-induced, stimulate antibody formation in irradiated mice for both corpuscular antigens. Exogenous viral-induced interferon had a much greater effect than the virus itself. This is probably explained by the dose dependence of the phenomenon. References 9: 4 Russian, 5 Western.
[210-6508]

UDC: 577.391:661.879

RESIDUAL DAMAGE AFTER INTERRUPTION OF CHRONIC EXPOSURE TO TRITIUM OXIDE AND EXTERNAL γ RADIATION

Moscow RADIOBIOLOGIYA in Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 19 May 80) pp 127-130

VORONIN, V. S. and MURZINA, L. D.

[Abstract] A study is made of the residual radiation damage in rats after interruption of long term administration of tritium oxide (HTO) in various daily doses and chronic γ irradiation in comparable daily and summary doses. The completeness of restoration of the hematopoietic system was also studied and the significance of its state in the formation of residual damage after chronic radiation exposure was estimated. The experiments were performed on 1600 male Wistar rats which received HTO orally for 3 months as described in an earlier work. Chronic γ irradiation was by ^{137}Cs. A clear variation of residual radiation damage as a function of the change in the number of myelokariocytes was noted for animals receiving HTO. In animals on the lowest dose, only the bone marrow cells showed this correlation. In animals exposed to γ irradiation the correlation was observed only in the lymphoid organs.
References 10: 7 Russian, 3 Western.
[210-6508]

UDC: 577.391:001.572

MATHEMATICAL MODELING AND CALCULATION OF DYNAMICS OF MOUSE POPULATION DEATH UNDER INFLUENCE OF IRRADIATION

Moscow RADIOBIOLOGIYA in Russian Vol 22, No 1, Jan-Feb 82
(manuscript received 14 May 80) pp 133-136

ROZENFEL'D, B. I., BUT, P. G. and CHIBRIKIN, V. M., Institute of Chemical Physics, USSR Academy of Sciences, Moscow

[Abstract] A study is made of the dynamics of death under the influence of radiation in 60 groups of white mice (males, 18-22 g) maintained under standard conditions but with natural illumination. Each group consisted of 20 individuals exposed to one time whole body γ radiation by ^{60}Co at 450 r, dose rate 44 r/min. Mathematical models based on the principle of random streams of events were used to describe the process of death of the animals with time. The dynamics of death of the animals in the groups is well described by a stochastic model with parameters dependent on the group. Social interactions within the group were found to be insignificant for the process of death of the

mice. The death process mimiced an epidemic, occurring intensively over a comparatively short period of time, 7 to 8 days, depending on the individual group of animals. References 6: 4 Russian, 2 Western.
[210-6508]

UDC 616-001.28-036.11-092.9-07:616.428-008.951-097.3

IN SITU MACROPHAGE-INDUCED FORMATION OF GLOBULAR ACCUMULATIONS OF AUTOLOGOUS ERYTHROCYTES IN LYMPH NODES OF DOGS WITH ACUTE RADIATION SICKNESS

Moscow ARKHIV PATOLOGII in Russian Vol 44, No 4, Apr 82 p 91

VLASOV, P. A., USSR Ministry of Health, Moscow

[Abstract] Investigations on outbred dogs irradiated with a minimum lethal dose of gamma rays showed that 7 days after irradiation rosette-like accumulations of erythrocytes with centrally located macrophages were evident in the cranial sinuses. The formation of these entities was regarded as the in vivo correlate of in vitro rosette formation, due to the known increase in anti-erythrocyte antibodies by the 7th day of radiation sickness and for which receptors exist on macrophages.
[229-12172]

UDC 616-001.28+577.164.3+612.115

COMPARATIVE STUDIES ON EFFECTS OF RUTIN AND FLAVONOIDS FROM THORNY CAPER ON RADIATION SICKNESS AND BLOOD COAGULATION IN RATS

Frunze IZVESTIYA AKADEMII NAUK KIRGIZSKOY SSR in Russian No 5, Sep-Oct 81 (manuscript received 10 Apr 81) pp 60-63

ALTYMYSHEV, A. A., OROZOV, M. A., VARVASHTYAN, V. M., GROMOVA, L. G., YARTSEV, N. M. and GORELKINA, O. I., Institute of Organic Chemistry, Kirghiz SSR Academy of Sciences

[Abstract] A study was undertaken of the physiological effectiveness of pharmaceutical-grade rutin and flavonoid extract of the thorny caper (ca.90% rutin) in rats with mild radiation sickness (250 R). The results showed that administration of rutin or of the extract (0.4 mg/100 g intraperitoneally) caused a decrease in body weight and an increase in the weight of the adrenals, concomitant with a decrease in the latter's ascorbic acid content. Administration of these preparations accelerated blood clotting in normal control rats and normalized it in the animals with radiation sickness. References 15: 12 Russian, 3 Western.
[241-12172]

UDC 576.353:591.044.82:591.481.1

AUTORADIOGRAPHIC STUDIES OF CELL KINETICS AFTER WHOLE BODY X-RAY IRRADIATION, PART 1: MODE OF DEATH OF LETHALLY INJURED PROLIFERATING SUBEPENDYMAL CELLS IN RAT BRAIN

Leningrad TSITOLOGIYA in Russian Vol 24, No 3, Mar 82
(manuscript received 5 Dec 80) pp 270-277

GRACHEVA, N. D., Department of Isotopic Research Methods, Central Scientific Research Roentgeno-Radiological Institute USSR Ministry of Health, Leningrad

[Abstract] Autoradiographic tests were performed on proliferating subependymal cells derived from the brain of Wistar rats treated with 3-H-thymidine, 60-80 min prior to whole-body x-ray irradiation with 50, 150, or 300 R. Evaluation of the time-dependent increase in the fraction of radio-labeled cells and the two-fold lower concentration of the label in pycnotic nuclei indicated that the lethally-injured cells which were irradiated in the early G_2 and S phases were subjected to mitotic, rather than interphase, death in the first post-radiation cell cycle. Such cells underwent mitosis ca. 2 h after irradiation, showing a 1 h lag phase vis-a-vis control cells, irrespective of the radiation dose. Figures 5; references 25: 14 Russian, 11 Western.
[242-12172]

UDC 576.353:591.044.82:578.087.317

AUTORADIOGRAPHIC STUDIES OF CELL KINETICS AFTER WHOLE BODY X-RAY IRRADIATION, Part 2: POSTRADIATION DEATH OF DIFFERENTIATING AND PROLIFERATING SUBEPENDYMAL CELLS IN RAT BRAIN

Leningrad TSITOLOGIYA in Russian Vol 24, No 3, Mar 82
(manuscript received 5 Oct 80) pp 278-285

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[Abstract] Post-radiation cell death in the subependymal zone of the rat brain was investigated by injection of 3-H-thymidine 60-80 min prior to X-ray irradiation of the animals with 50, 150, or 300 R. Subsequent correlation of autoradiographic findings with the cell cycle showed that the proliferating and differentiating (D) cells followed a fluctuating pattern in cell death, in that cells irradiated in the early G_2 and the S phases showed four peaks of mitotic cell death in the first postradiation cell cycle. Cells injured in the G_1 phase lost the capacity for DNA synthesis, since the 300 R-irradiated cells failed to incorporate 14-C-thymidine administered subsequently (3 h before

sacrifice, 12-17 h after 3-H-thymidine injection). Since these cells did not die within 4 h of irradiation, their death evidently came about during the first postradiation cell cycle. The cell death pattern of the D cells coincided with the death peaks and mitotic peaks of the proliferating cells, indicating that the D cells retained the rhythm and phase sequence of the mitotic cycle in the form of a short cycle. All the irradiated cells entered mitosis with a one hour delay, and the total number of cell deaths was dosage-related. Figures 4; references 11: 8 Russian, 3 Western.
[242-12172]

UDC 539.16.047:611/612

ENZYMATIC INDICATORS OF SKIN DAMAGE INDUCED BY EXTERNAL BETA-IRRADIATION

Yerevan BIOLOGICHESKIY ZHURNAL ARMENII in Russian Vol 35, No 1, Jan 82 (manuscript received 5 May 81) pp 36-41

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[Abstract] Factor analysis was conducted on the relationship between the severity of skin damage in outbred rats from external beta irradiation (^{85}Kr source, 30-100 gray dose) on the 14th post-irradiation day, and the activities of plasma and cutaneous enzymes in relation to dose and body weight. Analysis demonstrated that the most meaningful information, taking into consideration individual susceptibilities to irradiation, was provided by plasma and skin alkaline phosphatase, and lactate dehydrogenases, plasma hexose monophosphate shunt dehydrogeneses, and skin aspartate-aminotransferase. References 8: 4 Russian, 4 Western.
[317-12172]

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SOME DISTINCTIVE FEATURES IN FUNCTIONAL ACTIVITY OF THE CARDIOVASCULAR SYSTEM AND ADAPTIVE ANTIHYPOXIA MECHANISMS IN OPERATORS OF KEYBOARD COMPUTERS IN THE COURSE OF A WORK SHIFT

Moscow GIGIYENA TRUDA I PROFESSIONAL'NYYE ZABOLEVANIYA in Russian No 11, Nov 81 (manuscript received 1 Jul 81) pp 29-32

[Article by A. A. Kononeko and V. V. Derkach (Khar'kov), Institute of Industrial Hygiene and Occupational Diseases]

[Text] Our objective here was to examine some of the functional distinctions of the cardiovascular system, cerebral hemodynamics and manifestation of activity of adaptive antihypoxia mechanisms during work hours in operators at computer centers working with keyboard computers.

A hygienic study revealed that working conditions at the work places of computer center operators are not entirely favorable. For example, illumination at the work places is 100-150 lux lower than stipulated in the sanitary standards for this category of work. The level of noise, mainly in the medium and high-frequency spectrum, exceeds the maximum permissible level by 8-12 dB.

According to the time studies we conducted, the density of the work day for the operator group we surveyed constituted 74.5% for the main work and 11.8% for ancillary work.

The typical distinction of work of computer center operators is that it is necessary to maintain a high work pace, hold a working position for a long time, receive a significant amount of incoming information, perform a large number of similar "local" movements using muscles of the arm and hand.

We examined 23 computer center operators 20 to 32 years of age with work tenure of 2 to 10 years. All of the subjects were essentially healthy. We examined them 3 times during the work shift: before starting to work (0800 hours), before the lunch break (1200) hours and at the end of the shift (1700 hours) right at the operators' work places.

We determined pulse rate and arterial pressure by the method of N. S. Korotkov to assess the function of the circulatory system. We calculated the parameters of mean dynamic pressure (N. N. Savitskiy), stroke and minute volumes of circulation according to Starr, peripheral vascular resistance using the formula of Poiseuille and N. N. Savitskiy on the basis of the heart rate and arterial pressure.

Table 1.
Dynamics of pulse rate

Time of examination	M	Mean difference & error	P
0800 hours	71.5		
1200 hours	70.8	0.6±1.2	>0.5
1700 hours	66.8	4.6±1.2	<0.01

Table 2.
Dynamics of REG parameters

Time of exam.	Parameter	Lead: left frontomastoid	Lead: right frontomastoid
0800 hours	α	0.10±0.01	0.10±0.01
	$\frac{\alpha}{T}\cdot 100\ \%$	15.4±1.2	16.1±1.3
	$\frac{A}{h}$	2.0±0.1	1.7±0.1
1200 hours	α	0.12±0.01	0.11±0.01
	P	>0.1	>0.2
	$\frac{\alpha}{T}\cdot 100\ \%$	16.2±1.0	17.4±1.5
	P	>0.05	>0.2
	$\frac{A}{h}$	1.9±0.3	1.7±0.1
	P	>0.5	0
1700 hours		0.13±0.01	0.11±0.01
	P	<0.05	>0.2
	$\frac{\alpha}{T}\cdot 100\ \%$	16.4±0.8	18.7±1.7
	P	<0.05	>0.1
	$\frac{A}{h}$	1.8±0.3	1.6±0.1
	P	>0.5	>0.2

The changes in pulse rate of the subjects in the examined occupational group during the work shift are listed in Table 1, which shows that there was insignificant slowing of heart rate at the end of the first half of the work day, reaching statistical significance at the end of the shift.

Systolic arterial pressure dropped negligibly in the course of the work day, whereas mean dynamic and diastolic pressure did not change. We observed insignificant and statistically unreliable fluctuations of stroke and minute volumes, as well as peripheral vascular resistance.

In view of the above-mentioned changes in functional state of the circulatory system, it was interesting to compare the distinctions of cerebral hemodynamics in computer center operators.

We recorded rheoencephalograms [REG] directly at the operator's work place using a 4-channel 4-EEG-1 electroencephalograph with a rheographic attachment. The subject was seated in a relaxed position. Cerebral hemodynamics were examined using frontomastoid and bioccipital positions of electrodes.

The REG studies failed to demonstrate statistically significant changes in circulation in the posterior parts of the brain of computer center operators, so that we were able to limit ourselves to analysis of REG parameters for the left and right frontomastoid leads. We analyzed the following parameters of the REG in the course of the work shift: duration of anacrotic phase of the rheowave (α), ratio of α to the period of the entire wave ($\alpha/T\cdot 100\%$) and index of tonic tension (A/h). Table 2 lists the changes in these parameters of cerebral hemodynamics in the course of the work shift of

computer center operators. We observed an increase in both duration of the anacrotic phase of the rheowave and its ratio to the period of the entire wave, which reached statistical significance at the end of the shift in the left frontomastoid lead (see Table 2).

The absolute and relative increase in duration of anacrotic phase can be interpreted as manifestation of diminished volumetric rate of intracerebral blood flow in the left hemisphere (A. Ya. Mints and M. A. Ronkin; Kh. Kh. Yarullin, and others). At the same time, the absence of statistically significant changes in tonic pressure (see Table 2) does not warrant reference to increase in peripheral resistance of intracranial vessels.

Analysis of the submitted results of physiological studies shows that there are similar dynamics of systemic and intracerebral circulation, manifested by a tendency toward slowing of heart rate and reduction of volumetric blood flow rate in cerebral vessels of the dominant hemisphere.

Considering the above functional distinctions of the circulatory system, it was interesting to study the degree of activity of adaptive mechanisms that provide for proper delivery of oxygen to the body. The informativeness of the oxyhemometric method, combined in functional tests, in studies dealing with industrial hygiene has been demonstrated in the works of a number of authors V. N. Lyubartsev; A. N. Melkumyan and V. G. Knabengof; S. M. Rashman, and others). Nevertheless, there are very few such studies. Least studied are the dynamics of oxyhemographic parameters during mental work.

Changes in blood oxygenation were recorded on a type 0-36M oxyhemograph, using an ordinary sensor placed on the subject's earlobe. We recorded the oxyhemographic curves during the breath-holding test in expiration (Genchi test).

Of the oxyhemographic parameters studied--duration of stable A-B phase of the oxyhemographic curve, blood flow rate in the lung-ear segment, coefficient of recovery (A. G. Dembo, Ye. M. Kreps; E. Ya. Laane)--the most informative one was found to be the coefficient of intensity of hypoxic changes (CIHC), calculated with the formula:

$$CIHC = \frac{(A-D) - A - C}{A-C} \cdot 100\%,$$

where A is oxygen content of blood in expiration, C is oxygen content at end of breath-holding and D is minimum oxygen content during the hypoxic test. CIHC reflects the degree of activity of antihypoxia mechanisms and their ability to maintain oxygen equilibrium in the hypoxic phase (V. A. Nebotov).

As a result of these studies, it was demonstrated that there is a reliable increase in CIHC ($P<0.05$) at the end of the shift, as ompared to base values at the start of the shift. The demonstrated increase in CIHC is indicative of attenuation of activity of adaptive mechanisms directed at elimination of hypoxic changes during work of computer center operators.

A comparative analysis of the physiological parameters in question revealed that slowing of heart rate and intracerebral blood flow occurred against the background of diminished functional activity of adaptive antihypoxia mechanisms.

It can be assumed that the observed changes are instrumental in lowering work capacity and development of fatigue in individuals of the occupational group examined, and that they are largely determined by the inhibitory effect of hypokinesia and monotony on higher branches of the central nervous system.

Physiological and hygienic recommendations for optimizing working conditions of computer center operators were developed and tested in order to minimize the adverse effects of the work environment, primarily hypokinesia and monotony.

Use of lamps with fluorescent tubes providing at least 300 lux are proposed to improve the artificial illumination of work places. To lower the noise level in work rooms, the walls and ceilings should be covered with sound-proof panels.

The recommended schedule for work and rest of computer center operators includes warm-up exercise before starting to work, brief physical culture breaks lasting 2-3 min, which the operators perform individually in the course of the work shift, and physical culture sessions of 8-10 min 2-3 h after the lunch break.

Conclusions

1. In the course of the work shift of computer center operators, one observes slowing of heart rate, intracerebral blood flow and diminished activity of adaptive antihypoxia mechanisms.

2. In our opinion, the above physiological changes are the consequence of prolonged exposure to hypokinesia and monotony, which are inherent in the work of computer center operators.

3. A work and rest schedule for computer center operators aimed at overcoming the adverse effect of hypokinesia and monotony, as well as steps to improve sanitary and hygienic working conditions, have been developed.

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